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A.M.A. ARCHIVES OF SURGERY

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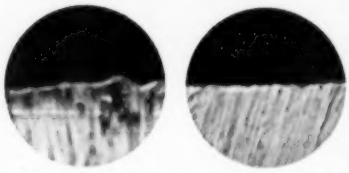

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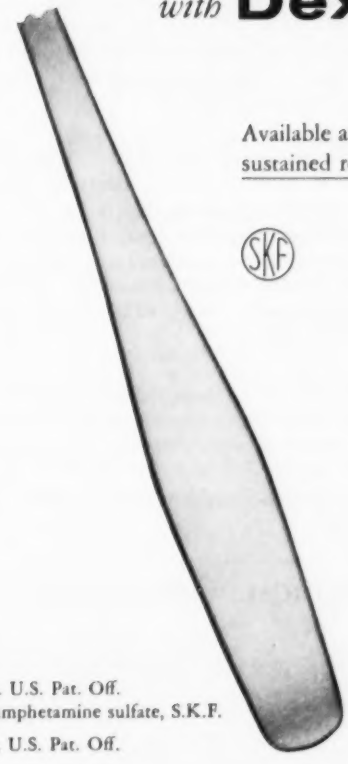

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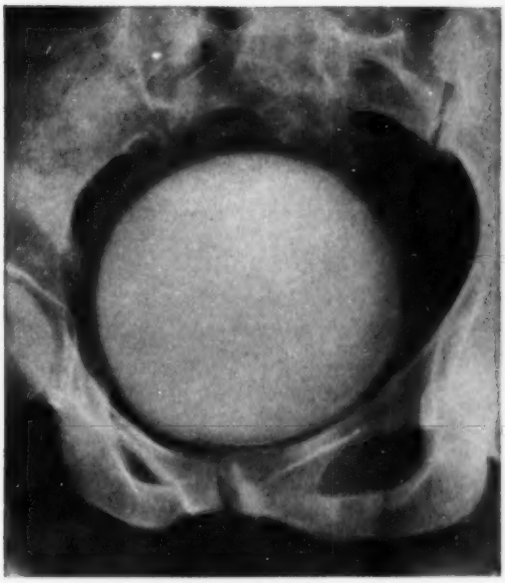

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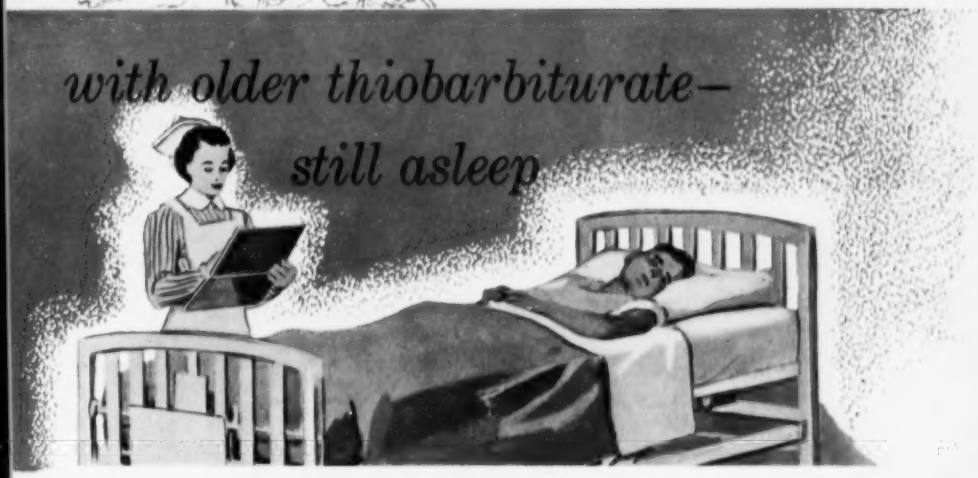

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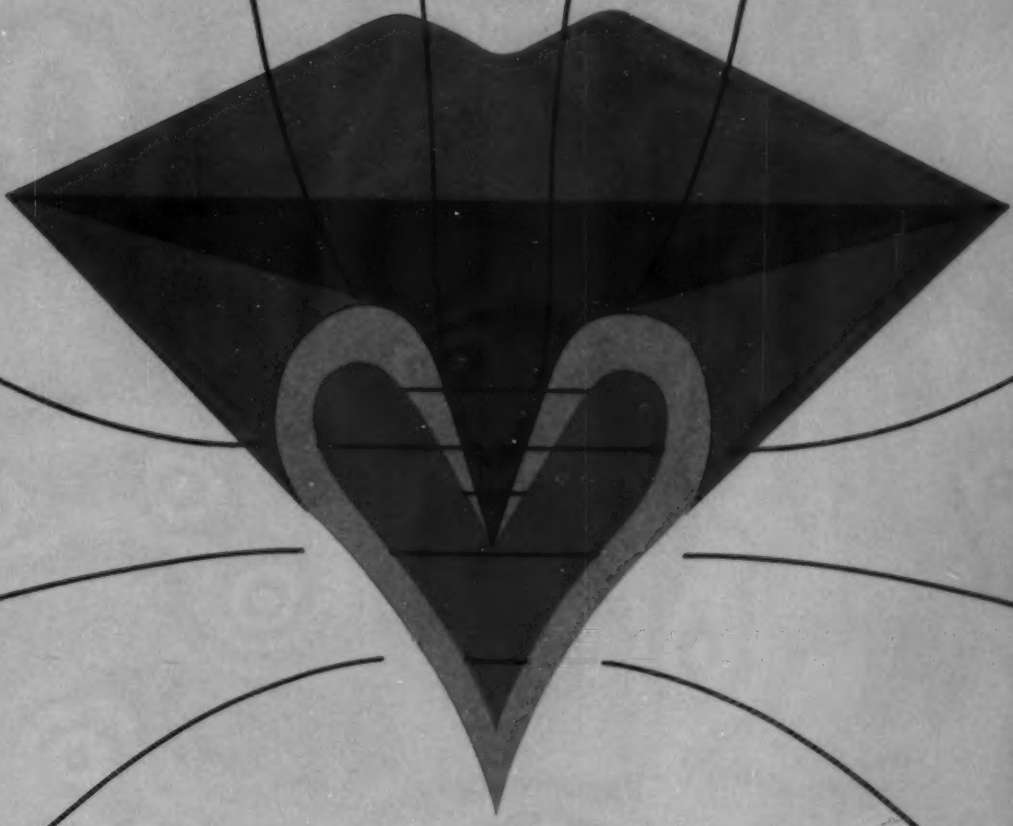

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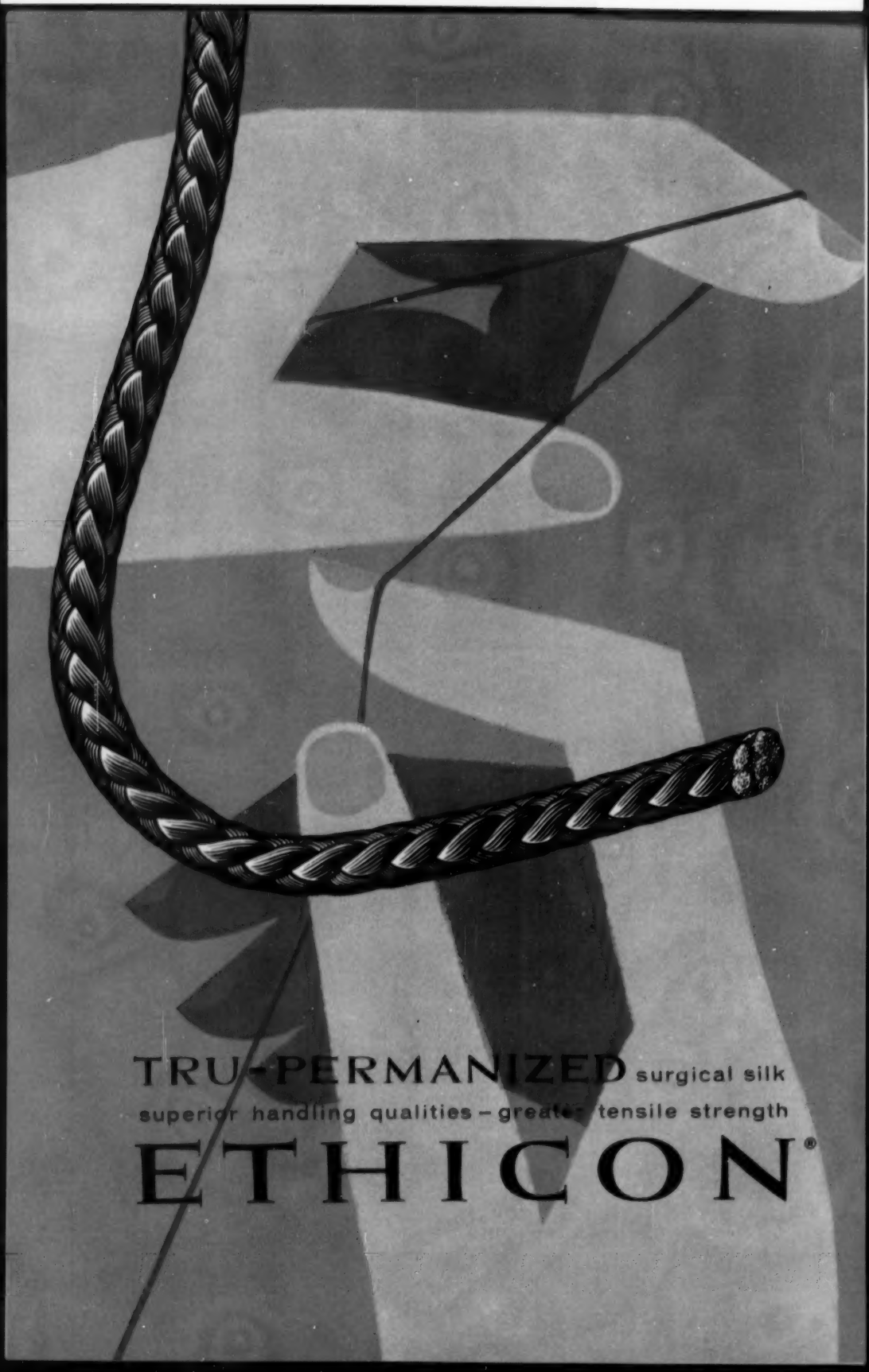
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The Changing Manner of Surgical Education

ROBERT M. ZOLLINGER, M.D., Columbus, Ohio

Since this is Washington's Birthday, I must tell the truth and admit that the flush of just pride on being elected president of this distinguished surgical society rapidly drained away as the time approached for me to prepare my remarks for you [here] today. This must have been apparent to our distinguished secretary, who has been a friend of long standing, since he never bothered to write for the title of my address. I would rather believe that he was secretly enjoying my dilemma than think that he did not want to detract from the otherwise fine program by inserting what he thought would most certainly be a very "dull title"!

I am not one to quote poetry or converse on a philosophical topic. I must therefore beg your indulgence, since I am going to discuss one of the subjects that is traditional in presidential addresses of surgical societies, namely, "The Changing Manner of Surgical Education."

A discussion of some aspect of current interest or conflict in regard to surgical training should be a part of every surgical society meeting. I have therefore deliberately chosen to discuss some of the present considerations in the education of the general surgical resident because I have sensed a certain amount of uneasiness over the country concerning more recent training requirements. Furthermore, I have gained the impression that many false rumors exist, including the myth that residency training in private hospitals will be gradually terminated and that only four-year programs in university centers will remain. Since this society geographically represents the core of this country and Canada, it is important that we keep well informed in these important matters. Our Canadian members are concerned, inasmuch as many of their young surgeons continue to meet the requirements for membership in the American College of Surgeons, as well as for examination by the American Board of Surgery.

I shall attempt to dispel some of the uncertainties and false impressions that have gained foothold since the time our training programs have been more closely studied by the Conference Committee on Graduate Training in Surgery and the professional experience of the individual young surgical applicant has been more thoroughly weighed by the American Board of Surgery. I should like to be so bold as to say that many of the misunderstandings arise because all too few surgeons concern themselves sufficiently with the problems encountered in the education of the young surgeon of today. There is too great a tendency to leave everything to the chief of the service, an appointed director of medical education, or the chairman of the intern and resident committee of the individual hospital. The fact is that everyone on the

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staff should be familiar with the pamphlet "Essentials of Approved Residencies and Fellowships," [1] prepared by the Council on Medical Education and Hospitals of the American Medical Association, as well as the latest booklet of information of The American Board of Surgery.[2]

There is an urgent need for medical evangelists to rekindle a feeling of keen responsibility in the individual surgeon in every hospital in this country for the education of his eventful replacement. Certainly no one escapes the moral obligation of taking part in the education of his successors. This was pointed out by the late Elliott C. Cutler [3] in a symposium on Undergraduate Teaching of Surgery, when he said, "for all doctors are thoroughly imbued with these lines of the Hippocratic Oath: 'to teach them this art if they shall wish to learn it.'" I think all of us are quite willing and anxious to assist in the teaching of the art and science of surgery, but we do not necessarily agree on how this is to be done in the most efficient manner. Stubborn adherence to long-established routines and traditions, as well as failure to appreciate the significant difference between residency training programs for service and programs for education, make the hard core of resistance to any proposed changes.

The backlog of young men, whose training was interrupted by our two recent wars and our continued global military obligations, made necessary certain modifications in our training programs. Many additional hospitals were approved for residency training, while others made room for more residents by affiliation with one or more neighborhood hospitals. In addition, short-, as well as long-term, basic science programs were instituted, and the practice of appointing an excessive number of residents was considered more a patriotic duty than a desirable pedagogic principle. Many of these changes brought about by the god Mars were good.

Those designated with the responsibility of evaluating the training opportunities being offered to our young surgeons determined after careful study that it was time to make certain realistic changes. Plans were formulated to end the era of the itinerant residents and the overpopulated resident staffs in many hospitals. Masters of surgery, long since departed to what we hope is the everlasting heavenly surgical seminar, (and there must be such a provision, since most of us can discuss little else), must look down upon their old services with despair at these overcrowded conditions. I have often wondered what they must be thinking as they see long lines of men in white uniforms rush from their beloved hospitals as the hour of 5 p. m. approaches. Perhaps some may have been deceived into believing that their hospitals had become great meccas of learning, attracting vast hordes of young men to their shrines. On the other hand, I suspect there are a few discerning souls who raise a note of discord in these celestial deliberations, as they more correctly compare this activity to a hive of bees—a swarm of drones doing their job, to be sure, as far as routine patient care is concerned. A few of the worker bees may be fortunate enough to spend some time buzzing around the research laboratory, delving into the queen bee's fantasy of the moment without losing eligibility time for Board examination. The majority of the remaining drones may sting the literature once to ensure reappointment, but, unfortunately, this is their dying effort!

In order that the necessity for revisions be properly understood, a review of the changing requirements by The American Board of Surgery over the 20 years of its existence should be profitable (Fig. 1). Originally, three years of hospital residency were required, but this requirement was lowered to two years in 1939, with a third year in basic science. Two additional years of preceptorship have always been required in this program before the candidate is accepted for examination by the

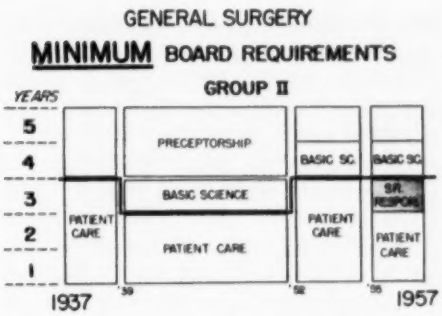

Fig. 1.—Under current requirements the year of basic science training is elective and may replace one year of preceptorship. This time devoted to basic science may be taken before, rather than after, the three years of clinical work.

Board. This pattern was followed for 15 years, until the year of credit for full-time courses in basic sciences was withdrawn in 1952 in favor of a return to three full years of clinical work. Pathology and basic sciences were to be integrated with the daily clinical training and were not to be organized as full-time assignments. Hospitals providing this type of program are classified as Group II.

After 10 years of the Board's existence, the Group I type of program, consisting of four years, was introduced in 1947 (Fig. 2). Three full years of hospital work were required, and, in addition, credit was given up to one year for full-time study in the basic sciences or in experimental surgery. In 1955 credit was no longer given for a full year of didactic work in the basic sciences. It was belived that a program approved for four years should have the facilities and environment for providing its own instruction in basic science rather than having the resident *in absentia* for a year in a postgraduate school. As a result, a number of hospitals were keenly disappointed when their program had to be readjusted from a four-year Group I program to a three-year Group II program. The Group I program, however, may continue to include as much as a six-month full-time assignment to surgical pathology. A year of nonclinical activity, such as an assignment to the surgical research laboratory, may be included in the program provided the resident is ensured sufficient clinical experience. Such an arrangement, however, should have the prior endorsement of the Conference Committee.

The deemphasis on the special full-time courses in basic sciences was done not because such courses were considered of little value but, rather, to ensure more clinical experience for the resident and, at the same time, to reemphasize the importance of the daily application of basic science to the management of the individual surgical patient. This is not a new point of view. The late Arthur Dean Bevan,[4] in 1935, said:

> I have found that, no matter how well trained the students have been in these daughter sciences of medicine before they come to us, it is absolutely essential to review these underlying sciences in each surgical case presented in the clinic.

While anatomy and pathology continue to form the backbone of the basic sciences in surgical training, with special examination time by the Boards, the other sciences have been included (Fig. 3). Any resident seeking competence or certification in general surgery must be able to apply not only anatomy and pathology but also physiology, pharmacology, bacteriology, biochemistry, and more recently, the principles of radioactivity. It is obvious that the daily application of these many basic sciences is necessary if their use is to become routine

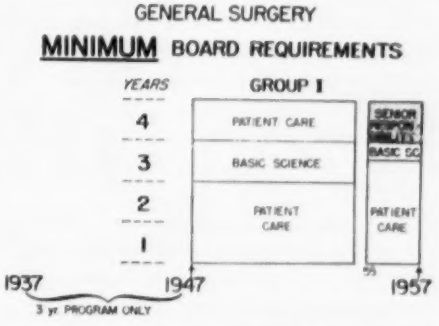

Fig. 2.—Six months' full-time assignment to a basic science subject (pathology or anatomy) is permitted on an elective basis. Senior responsibility in the fourth, or final, year is mandatory.

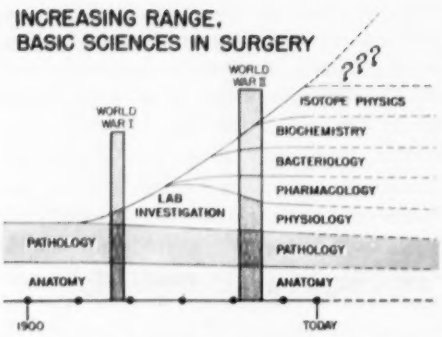

Fig. 3.—The progressive improvement in surgical care has paralleled the increasing application of the basic sciences.

by the young surgeon. Certainly no one will disagree that a lowered surgical morbidity and mortality will be the reward of such training. In summary, it may be said that time in basic science or surgical research is elective in the surgical training programs, but their daily application in clinical practice is strongly urged. Therefore, every program must develop a strong policy for the continual integration of the basic sciences into clinical teaching.

Since it cannot be denied that many hospitals are unable to offer the same opportunities in anatomy and the other basic sciences that are available in medical centers, there is a great responsibility on every surgeon to incorporate the principles of basic science in the daily care of his patients. One way to accomplish this is to use the blackboard in the operating room for the teaching of anatomy. The resident should be expected to sketch the essential anatomy of the scheduled operations for the next day. The surgeon and his team could then spend some time discussing the applied anatomy before, as well as during, the procedure.

That full-time assignments to pathology are no longer planned in the Group II programs in no way lessens the responsibility for continued instruction of the resident in this field. Again, the staff surgeon, as well as the hospital pathologist, has the responsibility of ensuring adequate opportunities for the weekly study of current pathology. In addition to death conferences, it is advantageous for the resident staff to submit in writing their diagnosis of the case to be discussed at the clinicopathological conference. Each week the pathologist should make available 10 or more current microscopic slides for study. The individual resident studies these slides sometime during the week and writes down his diagnosis and identification of the tissue involved. He is graded each week and a record maintained in order to measure his progress.

A study of the temperature chart in use by a hospital is a surprisingly valid indication of the emphasis placed on basic science information in daily practice. Adequate emphasis on such data may be assumed if approximately 50% of the chart is arranged for the recording of such essential data as fluids, electrolytes, and body weight. If, however, the graphic portion of this sheet for the recording of the temperature, pulse, and respiration consumes all of the space except for three or four lines at the bottom, it is time to assert one's responsibility to the resident staff by insisting that this antiquated form be revised.

Except for the changes in the basic science requirements, the introduction of the "senior-year" principle has probably created more discussion pro and con than anything since the Board of Surgery was organized (Fig. 4). The Board had found it difficult many times to determine just how

SENIOR YEAR PREREQUISITES FOR BOARD EXAMINATIONS

ASSIGNMENT	PROGRAMS	
	TYPE II (3 yrs)	TYPE I (4 yrs +)
ENTIRE YR. AT TOP LEVEL OF PROGRAM	GEN. SURG. PARENT HOSP	GEN. SURG. PARENT HOSP
SPECIFIC BEDS / SR. RES.	8 - 10	15 +
MAJOR OPERATIONS - GOOD VARIETY	200 +	300 +
SUPERVISION	STAFF	STAFF

Fig. 4.—During his senior year the resident must have full clinical responsibility under staff supervision.

much experience a young surgeon had had, especially if his training had been divided among several hospitals. Since in many surgical programs the resident did not gain a good variety of major operative work and full responsibility until his senior, or final, year, it was thought that every resident should have this senior year before being accepted for examination by the Board of Surgery. It is anticipated that the senior year in either a Group I or a Group II program will be devoted to general surgery in the parent hospital. Obviously, an exception should be made when there is a close group of hospitals united in a single program. It is a well-established principle that a specific allottment of beds should be officially designated by the hospital for the resident staff. While it is realized that some programs having limited clinical material graduate a far-better-trained surgeon than one having perhaps too much material, there is good reason to believe that the three-year programs should provide a basic minimum of 8 to 10 beds per senior resident in order to ensure a sufficient number of major operations of good variety during his period of training. A larger number of beds, 15 or more, has been suggested as desirable for each senior resident in a four-year program in order to provide an even greater number of major operations.[6] The resident should maintain an accurate log of the operations at which he has acted as first assistant, as well as those in which he was the responsible surgeon. The chief of the service should survey this list from time to time to make certain the resident has had a good variety of suitable operations. Finally, the resident in the senior year should have the entire responsibility for his cases under staff supervision. The senior-year principle will certainly tend to regulate the number of residents in a given program, since each man seeking Board certification must complete the full three years of a Group II program or the full four years of a Group I program. Since he must be given senior responsibility, it is obvious that neither his decisions nor his operative experience can be shared by a higher resident of five or six years' experience.

One of the controversial aspects of the senior-year principle involves the training programs organized to continue four years or longer. What about the eligibility of the resident who has completed four years of a program that has one or more chief residents at the five-, six-, or even seven-year level? If men in this type of program are to be dropped at the end of four years, it is essential that the program be organized in such a fashion as to ensure senior responsibility in their final year. Such services usually have an adequate number of beds to provide the fourth-year man with adequate operative experience and responsibility. One solution to this problem of ensuring senior responsibility for the fourth-year residents is to assign them a given service which admits tutorial patients to their care. A resident at the fifth-year or higher level directs the service from an administrative point of view, but his source of clinical material is independent of that of the fourth-year residents (Fig. 5). Since the administrative resident has already progressed through the senior year of responsibility, it is unnecessary for him to be particularly ambitious as far as operative experience is concerned. While the principle of responsibility in the senior year

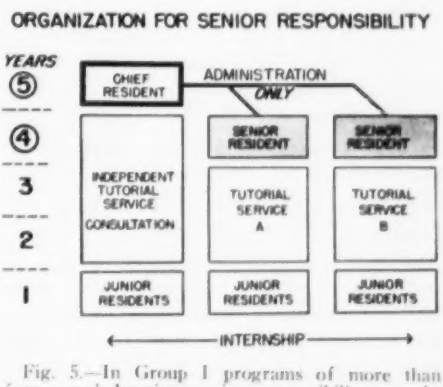

Fig. 5.—In Group I programs of more than four years' duration, senior responsibility may be offered to residents spending only four years by creating independent tutorial services.

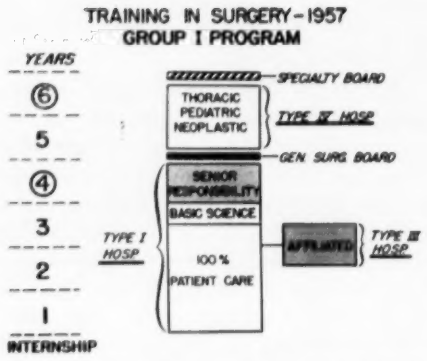

Fig. 6.—If specialty training is added to a Group I general surgical program, six years are required.

protects the individual resident, we must make certain that opportunities for more prolonged training are sustained, because these are absolutely essential in order to develop productive surgical research, as well as competent teachers.

Lastly, the new requirements prevent the transference of a resident to a surgical specialty program at the end of the third year of a four-year program (Fig. 6). He must now complete his full four years in order to gain senior responsibility and eligibility for Board examination. Such eligibility in general surgery is required prior to specialty training in such fields as thoracic, pediatric, or neoplastic surgery. Hospitals which are exclusively devoted to a particular specialty, such as pediatric, cancer, or thoracic disease, have been listed as Type IV hospitals. Such specialty centers may also be designated as Type III hospitals and provide one year in a surgical specialty provided they are affiliated with an approved Type I hospital program and can provide sufficient clinical experience for both types of residents. In the latter circumstance, such an affiliated Type III hospital is not approved for the final year of residency training. In some respects these affiliated programs in the past might well be compared to the farming system of the major baseball leagues. Some of the boys were gradually farmed out to the "sand lot leagues" until they had put in a sufficient number of years to request recognition for examination by The American Board of Surgery. On the other hand, certain promising "rookies" were rather quickly brought in from the "minor leagues" and given unusual opportunities in the mother institution. Obviously, there was a wide range of difference in the experience, abilities, and backgrounds of persons brought up in such training programs, making it very difficult for The American Board of Surgery to evaluate their individual potentials.

The resident in a Group II program has a definite advantage, as far as time is concerned, if he is planning to enter a surgical specialty that requires eligibility for general surgical board examination (Fig. 7). At the end of three years he has gained senior responsibility and may pursue a surgical specialty in a Type IV hospital. In this way his entire training period is completed in five years, in contrast to the six-year period required of the Group I resident who desires similar specialty training. If he does not enter such a specialty, he is required to spend either two full years of preceptorship or one year of the latter and one year devoted to the full-time study of more than one basic science.

From a review of the highlights in the present requirements for the training of the general surgical resident, it is obvious that

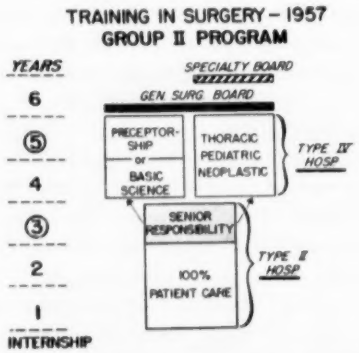

Fig. 7.—Eligibility to general surgical board examinations and two added years of specialty training may be completed in five years under a Group II program.

the right of appeal by either hospital or Board candidate should not be denied. Physicians do not like to be dictated to, nor do they submit to regimentation. The chiefs of surgical services are no exception. For these reasons, both the Conference Committee and The American Board of Surgery strongly support the idea that American surgery would be stifled by a rigid program which must be followed by every hospital. Hence, I see no cause for alarm, since I believe that these changes have already served a good purpose by focusing attention on policies of our training programs which have continued since World War II into our present state of high military preparedness.

In support of my feeling of confidence, it should be noted that at the present time there are 283 Group II and 246 Group I programs.[6] In addition, there are approximately 119 one- to two-year programs approved by the Council of the American Medical Association. Such programs are designed as preparation in general surgery before entering a surgical specialty. The effectiveness of these residency programs is evidence by the fact that the number of admissions to the American College of Surgeons, as well as certified specialists of The American Board of Surgery, has almost doubled since World War II. It is natural that this increase be the same for the College of Surgeons as for The American Board of Surgery, since their training requirements have been the same since 1949. It is obvious that we must further increase these figures if we not only are to train our replacements but also are to provide surgical care for the rapidly enlarging population. We must fulfill this obligation to posterity, regardless of the time and energy required of each of us.

Inflation and a booming economy have tended to have an adverse effect on the supply of tutorial cases for residency training. The inflationary trend should be considered when the requirements for admission of patients to tutorial services are established. Since there are too few "poor" people in these times, perhaps more consideration should be given to elevating the base line of financial responsibility in determining eligibility for admission to a tutorial service.

For the several reasons discussed. I should like to recommend for your serious consideration the formation of a permanent committee to study the problems of training in general surgery. Representation from each of the states, as well as the provinces of Canada within our geographic sphere of influence might be included. This should be a hard-working committee, which would give an annual report of its deliberations to the Association. Official interest on the part of this Association in the training of our successors would please the founders of this organization, would be consistent with our obligation as expressed in the Hippocratic Oath, and, lastly, would give tangible support to young men desiring surgical training and to the hospitals responsible for their education.

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Treatment of Fractures of the Hand

MICHAEL N. ZELENOCK, M.D.; ROBERT D. LARSEN, M.D., and JOSEPH L. POSCH, M.D., Detroit

In any presentation of the treatment of fractures of the hand, originality cannot be claimed, since many excellent articles have appeared in the literature previously.[1-4] However, the problem of education is always with us. This education applies not only to the residents on the staffs of the various hospitals but also to men who are not too familiar with the treatment of these fractures and to many others interested in the problem of trauma. The importance of the treatment of fractures of the hand need not be dwelt upon at this time except to emphasize the high morbidity associated with injuries of the hand. This fact alone necessitates continued research in this field. It has been stated repeatedly that the time lost from work in industry is greater for treatment of fractures of the hand than it is for treatment of fractures of the long bones. It is important to restore the human hand to as good a functioning unit as possible following trauma to the bone of the hand. Effort utilized in obtaining anatomical reduction of these fractures will be rewarded in the restoration of function and cosmetic results obtained. The problem of muscles and soft tissues between the bone ends is not present in the hand, as it is in the long bone; however, angulation at the fracture site, rotation of the distal fragments, adhesion of the flexor tendons, and stiffness of the joints are all problems one must contend with. It has been stated that a 15-degree angulation in the proximal phalanx will prevent the tip of the finger from reaching the palm. In addition, it is said that the hand cannot be slipped into a narrow space because of loss of extension when there is a 15-degree palmar angle motion. A few degrees of rotation results in the fingers crossing when they are flexed into the palm.[5]

It is the purpose of this paper to present problems encountered in dealing with a series of 119 cases and 170 fractures encountered at the City of Detroit Receiving Hospital and 142 cases encountered in private practice.

Isolated Fractures

Although attempts have been made to treat these fractures in the simplest way possible, we have not hesitated to use fixation with Kirschner wires when indicated. Fractures of the distal phalanx are usually the result of direct, crushing violence, sustained, for example, by punch presses, car doors, lawn mowers, and so on. Associated subungual hematomas are best drained early—occasionally pulp hematomas occur and may necessitate early drainage. Usually there is marked comminution with little displacement of the distal phalanx. Such a fracture can be immobilized on a curved metal splint or plaster splint. A rather frequent fracture involving the distal phalanx, the so-called mallet, or baseball, finger, consists of avulsion of the bone fragment at the insertion of the extensor tendon (Fig. 1). In addition, fractures involving the volar aspect of the distal phalanx at the insertion of the flexor digitorum profundus, although rare, are encountered (Fig. 2). If the fracture is seen early, open reduction may be carried out immediately by suturing the fragment in place. The ruptured extensor tendon with the displaced fragment of bone may be

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Department of Surgery, City of Detroit Receiving Hospital, and the Wayne State University College of Medicine Service, Grace Hospital.

Fig. 1.—Ruptured extensor tendon showing fragment of bone torn loose from the distal phalanx.

treated also by placing the distal phalanx in hyperextension and the middle phalanx in flexion. This may be done with a molded plaster splint. Reduction may also be maintained by a Kirschner wire placed longitudinally through the joint and into the proximal phalanx. In delayed cases, it is probably better to remove the bone fragments and suture the tendon to its insertion in the distal phalanx.

Occasionally in patients who have severe injury to the distal phalanges, adequate reduction may be obtained by repairing the soft-tissue injury and maintaining a reduction by means of intramedullary placement of a small Kirschner wire or a small needle from the distal phalanx into the proximal phalanx (Figs. 3, 4). Permanent stiffness of the joint is rare if these Kirschner wires are removed within four weeks.

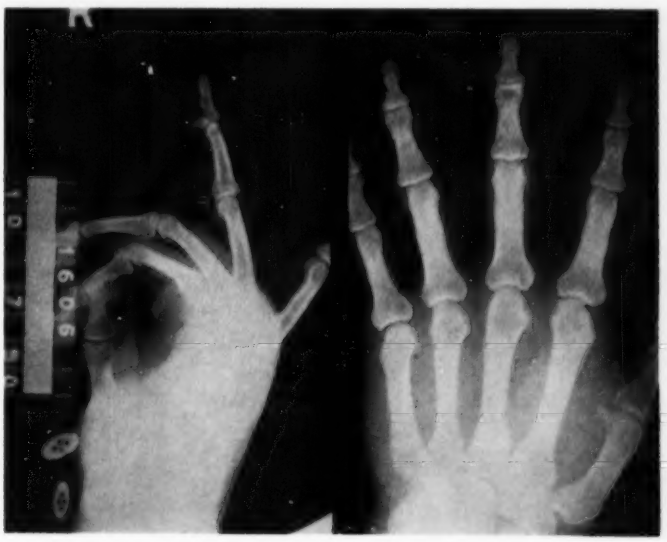

Fig. 2.—Severe injury to the flexor surface of the middle finger, illustrating a rupture of the flexor digitorum profundus with avulsion of a small fragment on the volar aspect of the distal phalanx.

Fig. 3.—Severe traumatic amputation of the distal phalanx of the right middle finger incurred on an automobile fan. (Rings, of course, are removed as soon as the patient is seen, to prevent injury to the finger bearing it.)

Dislocation at the distal interphalangeal joint on the volar aspect of the finger may occur. This is occasionally seen in severe baseball injuries. Usually the wound is open in nature, and one can readily obtain reduction with the patient under adequate anesthesia.

In severe injuries of the distal interphalangeal joint, a useful digit may be obtained by arthrodesis of the joint in position of function (Figs. 5, 6). Not infrequently with injuries involving the distal phalanx, injuries to the nail and nail bed also occur. The nail may be left on at the time of the original injury for protection; however, if severe deformity of the nail does occur, it is probably better to remove the nail in its entirety along with the nail bed and apply a skin graft. This procedure is often quite difficult, and occasionally it is necessary to reoperate on the patient several times to remove all of the nail bed.

The immobilization period for fractures of the distal phalanx is usually three to four weeks.

Displaced fractures of the middle phalanx depend on action of the tendon of the flexor digitorum sublimis as related to the fracture site. If the fracture is proximal to the insertion of the tendon, dorsal angulation occurs. Volar angulation is present when the fracture occurs distal to the insertion of the flexor digitorum sublimis (Fig. 7). Transverse fractures may be reduced and mobilized in a curved plaster splint for three to four weeks. However, unstable, oblique, or comminuted fractures may require traction over a curved splint

Fig. 4.—After repair of the soft tissues, immobilization was maintained by means of a small Kirschner wire placed obliquely across the injured area.

to restore position and length. Severely injured open fractures may be pinned (Fig. 8).

Fractures of the proximal phalanx are usually transverse in nature, although they may be oblique or comminuted. Reduction can be obtained by manipulating the fragments into position and mobilizing them in a plaster forearm splint with the metacarpophalangeal joint in moderate flexion—20

Fig. 5.—Severe injury to the distal interphalangeal joint of the little finger with resultant flexion deformity.

to 45 degrees of flexion and the interphalangeal joints at 45 degrees. Owing to the action of the interossei and lumbricales, more angulation of the fracture occurs, and reduction is accomplished by flexion of the distal fragments on the proximal fragments (Fig. 9). Unstable, oblique, or comminuted fractures will require traction over a curved splint. Healing often takes place within 21

Fig. 6.—Because of the severe injury permanent arthrodesis was done by employing small Kirschner wires.

days, and traction can be removed. Early motion without angulating the fracture site is important to restore function at the metacarpophalangeal joint. In a reduction of these fractures, the finger tips should be drawn toward the tubercle of the navicular (scaphoid) bone to prevent rotation of the bone fragments, with resulting angulation. Simple skin traction may be used with good results (Figs. 10, 11). If there is any doubt about obtaining adequate reduction, or if an open fracture is present and is seen early, small Kirschner wires may be

Fig. 7.—Anatomical principles involved in injuries to the middle phalanx. If the fracture is proximal to the insertion of the flexor digitorum sublimis tendon, dorsal angulation occurs. Volar angulation is present when the fracture occurs distal to the insertion of the flexor digitorum sublimis tendon. (From Bunnell, S.: Surgery of the Hand, Ed. 3, Philadelphia, J. B. Lippincott Company, 1956.)

Fig. 8.—In severe fractures of the middle phalanx, especially the soft-tissue injuries, immobilization can be obtained by means of small Kirschner wires, avoiding the joints.

placed at right angles across the fracture site to obtain proper immobilization (Figs. 12, 13). One should be extremely careful that pressure necrosis does not occur on the volar aspect of the finger, as illustrated in Figure 14. Fracture dislocation about the

Fig. 9.—Drawing illustrating actions of the interossei and lumbricales muscles, causing volar angulation of the fragments in a fracture of the proximal phalanx. (From Bunnell, S.: Surgery of the Hand, Ed. 3, Philadelphia, J. B. Lippincott Company, 1956.)

proximal interphalangeal joints is extremely troublesome. Adequate reduction is necessary; and if this cannot be obtained by closed manipulation, then the method of using three Kirschner wires transversely in the phalanges, as advocated by Bunnell, gives excellent results. Here, two wires are placed in the middle phalanx and one in the proximal phalanx. The distal wire is pulled straight distally to separate the joint ends. The proximal wire near the joint is presented in volar direction, while the third wire in the proximal phalanx is pulled dorsally. We have used this method in three cases, with excellent results. In our hands, capsulectomies and arthroplasties about the proximal interphalangeal joint usually do not result in marked improvement.

Dislocations about the metacarpophalangeal joint are rare but may occur. Usually the joint injury is so severe that permanent

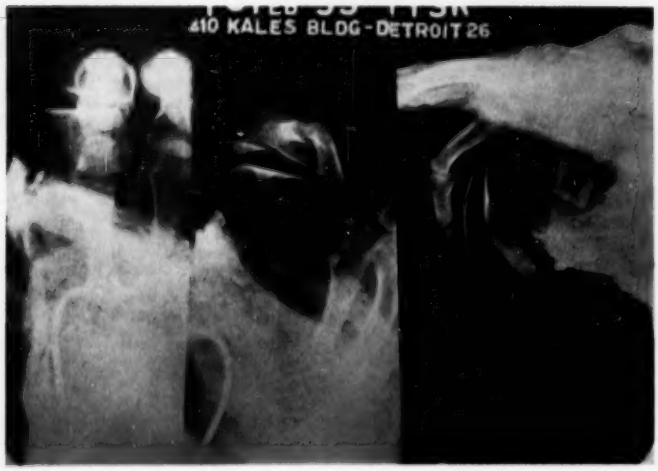

Fig. 10.—Transverse, slightly comminuted fracture of the proximal portion of the proximal phalanx, immobilized on a curved metal splint.

Fig. 11.—Healing in fairly good position as noted approximately two months after the original injury.

stiffness does result. In the ones we have encountered it was necessary to perform arthrodesis at the metacarpophalangeal joint (Figs. 15, 16).

Fractures of the first metacarpal, that is, those involving the thumb, are usually present in the proximal one-third and may or may not be associated with dislocations at the greater multangular bone, the so-called Bennett's fracture. Reduction is best accomplished by traction with a pin in the proximal phalanx of the thumb, as shown in Figures 17 and 18. Failure to obtain good reduction by traction will require open reduction and fixation of the fragments with Kirschner wires, as shown in Figures 19 and 20.

Fig. 12.—Traction obtained by means of a small Kirschner wire placed transversely through the distal portion of a fractured proximal phalanx.

Fractures through the neck of the metacarpal bone are the commonest fractures of this bone. The head is usually rotated into the palm (Fig. 21). These can easily be reduced after the impaction, if present, has been broken up by 90-degree flexion of the proximal phalanx and pressure applied dorsally. The fracture reduced in this manner should not be splinted in this position, with phalanges acutely flexed. More frequently than not a permanent flexion deformity occurs. Once, after repeated unsuccessful attempts elsewhere to correct this deformity in a patient who had been referred to us, amputation of the finger was necessary. The fracture is unstable, and position is lost when pressure is released. Good results may be obtained by intramedullary fixation with a Kirschner wire or wires just radial to the extensor tendon on the dorsal surface of the metacarpal head,

Fig. 13.—Excellent healing in good position. The flexor digitorum profundus did not become adherent to the callus. Some stiffness persists, but this is not severe.

Fig. 14.—Complete destruction of the soft tissues and partial destruction of the flexor tendons of the proximal phalanx of the right ring finger. Strong steady traction was placed over a roller gauze for five weeks. When he was first seen, the patient had the appearance shown in the photograph. By means of sliding pedicle grafts from each side of the finger, adequate covering was obtained. The fracture had not healed when the patient was first seen, but it eventually did heal in fairly good position, although attention was directed to the soft-tissue destruction. A fairly good functioning finger resulted.

Fig. 15.—A transverse fracture of the fifth metacarpal with dislocation of the metacarpophalangeal joint of the ring finger.

Fig. 16.—Fracture of the fifth metacarpal reduced with small Kirschner wires. It was impossible to get a good reduction of the metacarpophalangeal joint. Adequate reduction was obtained with small Kirschner wires. Permanent stiffness is present in this joint.

Fig. 18.—This fracture was treated with wire traction placed through the distal portion of the proximal phalanx. Adequate reduction was obtained.

Fig. 17.—Bennett's fracture involving the base of the first metacarpal.

Fig. 19.—An old injury to the base of the first metacarpal.

Fig. 20.—Open reduction was carried out, and small Kirschner wires were inserted.

and the insertion must be made with the metacarpal joint in full flexion (Fig. 22). In this way the greater part of the extensor tendon mechanism is avoided by the pin, and full flexion after pinning is allowed. This can be accomplished by opening the fracture site; or when there is lateral displacement, the fracture site may be opened

Fig. 21.—Typical view of a so-called boxer's fracture with volar angulation of the head of the metacarpal.

and the wire placed through the head and then driven down the medullary canal of the proximal fragment after reduction has been obtained. The advantage of this kind of treatment is that the other fingers are free to move, as are the finger joints of the involved finger. Adequate reduction is obtained.

Fig. 22.—Reduction was obtained by means of small Kirschner wires placed longitudinally through the fractured site. Actually, one Kirschner wire is sufficient to obtain reduction.

Fig. 23.—Typical deformity caused by the action of the extensor carpi tendon and the interosseus muscles and a fracture of the shaft of the metacarpal. (From Bunnell, S.: Surgery of the Hand, Ed. 3, Philadelphia, J. B. Lippincott Company, 1956.)

In fractures of the shaft of the metacarpal, typical deformity is caused by action of the interosseous muscles; in addition, the position of the flexor carpi ulnaris and flexor carpi radialis on the proximal portion of the metacarpals often causes interesting deformities (Fig. 23). Adequate reduction of a fracture of the shaft of the metacarpal may be obtained by placing a small Kirschner wire transversely through the distal portion of the proximal phalanx and applying traction over a simple support. In addition, adequate results may be obtained by first reducing the fracture and then placing a Kirschner wire at right angles through the fractured metacarpal into the adjoining metacarpals, which have not been fixed. Two or three wires may be necessary for this procedure. If attempts at closed re-

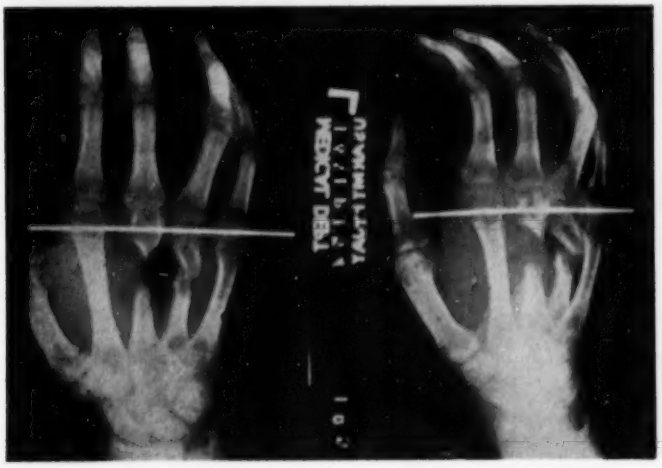

Fig. 24.—Severe gunshot wound of the hand in a soldier with soft-tissue destruction and loss of portions of the shaft of the third and fourth metacarpals. Proper alignment of the fragments was obtained by means of a Kirschner wire placed transversely through the heads of the metacarpals.

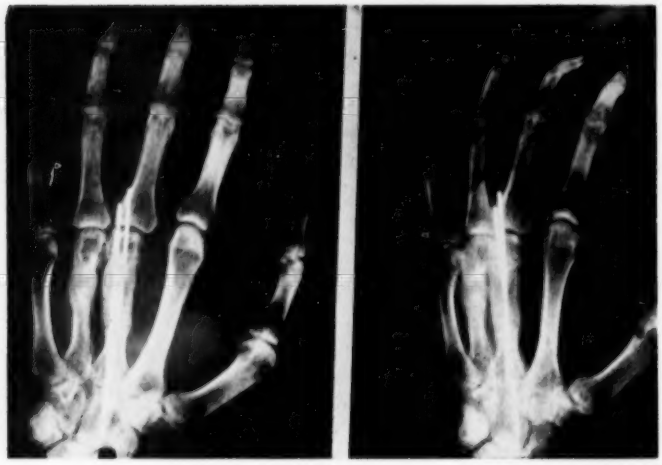

Fig. 25.—Subsequently bone-grafting procedures were done employing cortical bone and maintaining immobilization with Kirschner wires placed longitudinally through the remaining portion of the bone and the bone graft.

duction fail, or if one is presented with an open wound to begin with, then small Kirschner wires can be placed at right angles across the fractured shaft with good results. These wires may or may not be removed in the future. Fractures at the base of the metacarpal without dislocation with carpal bone are usually well treated with immobilization, and they usually heal uneventfully.

Multiple Fractures

With the present-day use of the large punch presses, power saws, and so on, one many times sees severely crushed hands with multiple fractures rather than the isolated fractures described above. These severe crush injuries are usually open in nature. In these severely crushed hands one has to contend not only with fractured bones but also with avulsed skin, lacerated tendons, destroyed nerves, and injured blood vessels. In this type of injury it is needless to say that adequate hospital facilities must always be utilized. The operative procedure is always done in a well-equipped operating room under adequate anesthesia. Débridement is done and is of limited nature. We do not hesitate to insert Kirschner wires in an open wound to ob-

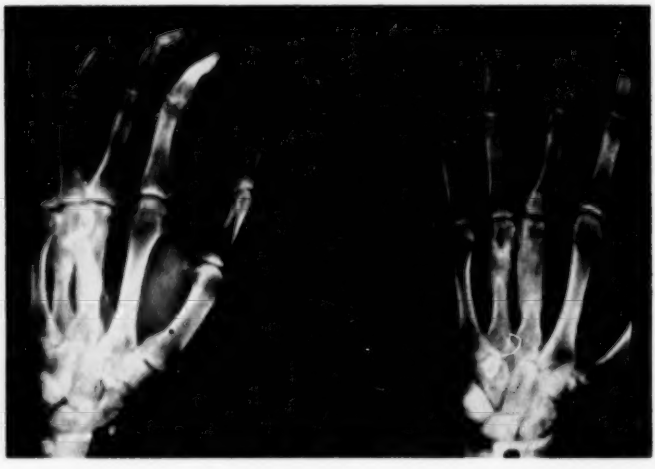

Fig. 26.—Good healing of the bone graft. The patient has excellent-appearing metacarpals.

Fig. 27.—Postoperative view shows good flexor power noted in all of the fingers.

Fig. 28.—A severe saw injury in a 65-year-old lumber employee with destruction of phalanges in the thumb and middle and ring fingers.

tain adequate reduction of the fracture site, and at no time have we seen any reaction from the Kirschner wires themselves. After carefully débriding the wound and irrigating it thoroughly with saline, with removal of all foreign bodies and all dead muscle, adequate skin closure must be accomplished. The skin should be closed under normal tension; however, if too much tension is needed, then skin-grafting procedures should be carried out. This may be in the nature of a sliding pedicle graft, with the utilization of a split-thickness skin graft to cover the area where the pedicle has been removed. If necessary, an abdominal pedicle may be applied immediately. If severe

Fig. 29.—Soft-tissue injury encountered in this patient. There has been complete destruction of the proximal phalanx of the thumb. In addition, the ring finger was hanging only by skin. This finger was filleted, and the skin was used to cover a large defect on the volar aspect of the middle finger.

edema has occurred immediately after the injury, we have used hyaluronidase directly into the edematous area with good results. The universal metal splint, as recommended by Mason and Allen,[9,10] is useful in the severe crush injuries where all of the fingers of the hand are involved; we are,

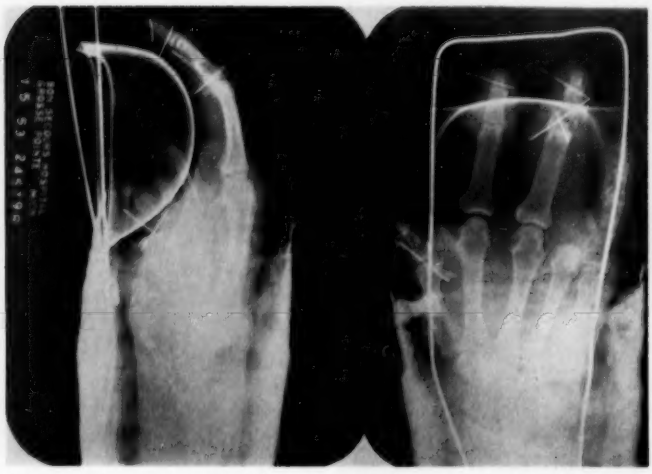

Fig. 30.—Postoperative x-rays showing the utilization of small Kirschner wires to unite the distal phalanx of the thumb to the first metacarpal. In addition, the middle finger is preserved with several small Kirschner wires to maintain healing of the soft tissues. Pulp traction was obtained by inserting No. 22 needles through the distal phalanges of the fingers. The entire hand was then dressed on a universal metal splint. This splint and a metal rod were incorporated in plaster, and traction was then applied to the index and middle fingers.

however, inclined to agree with Curry,[11] who thinks that each fracture should be individualized. We do not like to use this splint when only one finger has been injured, since resultant stiffness may occur in the other fingers. If use of the universal metal splint does not appear to be feasible, traction may be obtained by placing small Kirschner wires in the bones distal to the fracture area and applying traction to either a metal coat hanger or brass soldering iron (brazing wire). We have discontinued the habit of immobilizing these over a roller bandage, because many times the fingers become quite stiff and never again straighten out. A larger ball is preferable to a small roller gauze. This would be the size of the head of the universal metal splint. Adequate immobilization, of course, should be checked by repeated x-ray exam-

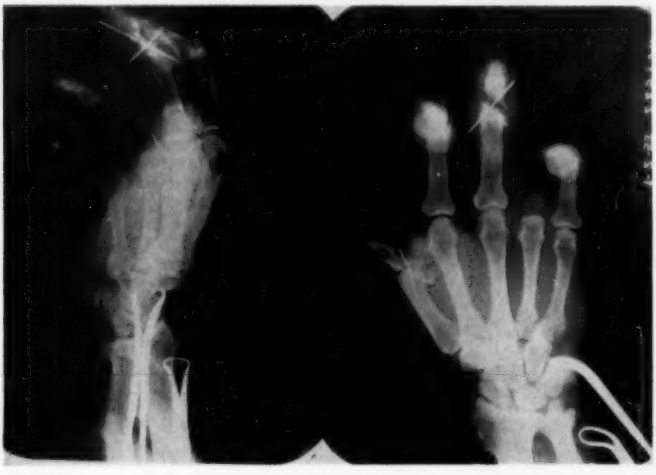

Fig. 31.—Postoperative x-ray showing the nonunion present in the middle phalanx. The position of the proximal phalanx in the thumb is maintained.

Fig. 32.—Flexion possible postoperatively.

Fig. 33.—Extension possible postoperatively.

ination. Usually, after five or six weeks, the fracture will be healed well enough so that the traction and splint may be removed and adequate physical therapy methods instituted.

We do not hesitate to suture extensor tendons with fractures of the phalanges or metacarpals; however, we usually find that if flexor tendons are sutured at this time they do adhere to the callus formation and necessitate further tendon-grafting procedures. Therefore, a secondary tenorrhaphy or tendon graft is usually the procedure of choice. Lacerated nerves should be sutured at the time of the primary treatment.

Illustrative Cases

The treatment of these severe crush injuries and open fractures described above can best be illustrated by two case histories.

CASE 1.—A soldier had suffered a severe gunshot wound of his hand. After initial débridement and preservation of all possible viable tissue, a small Kirschner wire was placed transversely through the heads of the metacarpals to maintain the normal architecture of the hand. Subsequently a pedicle graft was placed to the dorsal aspect of the hand. Bone grafts utilizing cortical bone with Kirschner wires were used to maintain the largest graft in good position with the normal bone. Good healing of the fractured areas resulted, and the patient had a good functioning hand (Figs. 24, 25, 26, 27).

The next case, reported in detail, illustrates many of the problems encountered in crush injuries.

CASE 2.—"A 65-year-old man, a lumber worker, suffered severe multiple fractures and lacerations of his right hand when it was caught in a shaver while he was at work. Examination revealed open fractures with loss of bone substance of the thumb and index, middle, and ring fingers. In addition, there was laceration of the little finger.

"The patient was admitted in shock and was given 500 cc. of whole blood and 500 cc. of plasma before coming to the operating room. At the beginning of surgery his blood pressure was 140/80. Anesthesia was satisfactorily obtained by means of nitrous oxide and intravenous thiopental (Pentothal) sodium. The blood pressure cuff was placed on the upper arm and used as pneumatic tourniquet to avoid excessive bleeding. The entire hand was thoroughly washed with pHisoDerm* and water and irrigated numerous times. Sterile drapes were placed in the usual manner. Examination of the thumb revealed multiple severe lacerations, with only the medial vessels and nerves intact. There had been practically complete loss of the middle phalanx except for a small portion, measuring 1×1 cm., that articulated with the distal joint. This was removed. The flexor tendon was identified, cut short, and allowed to retract proximalward. The extensor tendons were likewise débrided. The distal phalanx appeared to be viable; so this was united to the metacarpal by two small

*An emulsion containing entsufon (sodium octylphenoxyethoxyethyl ether sulfonate), hydrous wool fat U. S. P., cholesterols, lactic acid, and petrolatum.

Fig. 34.—Pathological fracture in an enchondroma in the proximal phalanx of the right little finger. The patient did not know that this enchondroma was present; however, when she bumped her finger, x-rays were taken and the pathological fracture was discovered.

Kirschner wires. A true arthrodesis was not done, but the distal phalanx was just united to the metacarpal bone. There were multiple lacerations around the head of the metacarpal and also at the base of the nail. All of these were carefully closed with interrupted No. 60 cotton sutures and 00000 nylon sutures. Examination of the little finger revealed that there was merely a superficial laceration over the middle phalanx. This was carefully irrigated and closed with interrupted 00000 nylon sutures.

"Examination of the ring finger revealed that there had been a severe open comminuted fracture of the middle phalanx with loss of bone substance and, in addition, there had been a severance of the flexor tendons. The digital vessel on the lateral aspect likewise had been severed, along with the digital nerve. Examination of the middle finger revealed that there had been a severe compound comminuted fracture, with loss of bone substance of the middle phalanx. The flexor digitorum sublimis had been severed, as had the flexor digitorum profundus at the distal portion of the middle phalanx. All the skin on the medial side of the finger had been avulsed. Therefore, since the ring finger had been so severely destroyed, the bone was removed along with the extensor mechanism, and the skin was preserved and then sutured to the side of the middle finger. This provided an immediate full-thickness pedicle graft to the middle finger. The remaining portions of the bone of the middle finger were united by means of two small Kirschner wires. There had been a good deal of loss of bone substance, so that the bones were in good position, but not approximated.

"The index finger had likewise suffered a severe open fracture of the middle phalanx with multiple lacerations. These lacerations were all carefully cleansed and closed with interrupted 00000 nylon and No. 60 cotton sutures.

"During the procedure the wounds were all carefully irrigated numerous times with saline. A check x-ray taken in the operating room revealed the fragments to be in good position. The hand

Fig. 35.—Fracture treated by excision of all of the cartilaginous material. The wound was packed with bone chips, and a bone graft was used to maintain good reduction. Excellent function resulted.

was dressed in a modified pressure dressing on the universal metal splint, and traction was applied to the index and middle fingers by inserting two No. 22 needles through the tips of these fingers and applying rubber-band traction to metal on the universal metal splint, which was then incorporated in the cast.

"During the operation the patient's blood pressure rose to 180 mm. He was returned to the floor in good condition."

Although the patient had mild diabetes, his postoperative course was uneventful, and one week later he was again brought to the operating room; this time, under sterile precautions, without anesthesia, the dressing to the right hand was removed. The lacerations were all found to be healing well. Some of the sutures on the dorsal aspect of the hand were removed. The thumb was viable, although at the time of the original procedure there had been some doubt in our minds as to whether or not it would survive. A modified compression type of dressing was then reapplied. Traction was again placed on the index and little fingers. The universal metal splint wire that had previously been applied to the upper extremities was left intact.

Two months following the original surgery, the Kirschner wires were removed from the thumb, leaving the patient a fairly good thumb to work against. Stiffness in the index and little fingers persisted, but he was gradually able to bring them toward the palm. While the patient was hospitalized, he developed a subdeltoid bursitis (this was undoubtedly due to the fact that his arm was in a sling while he was hospitalized). At times the middle finger gave him a good deal of discomfort because of the nonunion of the fracture of the middle phalanx. It was recommended that bone-grafting procedures be carried out; however, this was never done.

The patient, of course, was unable to use his hand for skilled work, but he got along quite well (Figs. 28-33).

Fractures may also occur in tumors of the hand, especially in endochrondomas. It is estimated that pathological fractures may occur in up to 25% of the cases. Many times the first symptom of a fracture is noted in one of these tumors. Excision may be done of all the cartilaginous material present and the defect filled with bone chips. In addition, a bone graft may be used (Figs. 34 and 35).

TABLE 1.—*Age and Sex*

Males	107
Females	35
Youngest	2½ mo.
Oldest	86 yr.

TABLE 2.—*Etiology*

Machines and presses	40
Baseball	13
Doors	13
Falling objects	11
Falls	11
Saw injuries	10
Miscellaneous	44

Summary

A series of fractures of the hand involving 261 patients has been analyzed. Of these patients, 119 were hospitalized at the City of Detroit Receiving Hospital, and 142 were seen on private services. The ages in the series of 142 cases varied from 2½ months to 86 years. There were 107 males and 35 females (Table 1). Etiological factors were many and varied (Table 2). However, heavy punch presses and large-machine accidents caused the most serious injuries. Farm accidents, automobile injuries, and so on, all are agents in causing these injuries.

TABLE 3.—*Immediate and Delayed Treatment*

Primary repair	95
Secondary repair	45
Unclassified	2

The majority of the fractures were seen primarily. The cases that were seen secondarily had some complicating factor and were referred because of this condition. The bones fractured are listed in Tables 4 and 5. Twenty-eight of these fractures involved more than one bone, and nine of them were severe crushing injuries that required multiple procedures. Joint dislocations with or without fracture of the adjacent bone gave considerable difficulty (Table 6). Dislocated distal interphalangeal

TABLE 4.—*Fingers—Bone Fractured*

Distal phalanx	46
Middle phalanx	34
Proximal phalanx	41
Metacarpal	38

TABLE 5.—*Thumb—Bone Fractured*

Distal phalanx	14
Proximal phalanx	11
Metacarpal	5

joints usually had considerable soft-tissue injury, especially to the extensor tendon mechanism. Proximal interphalangeal joints, especially those involving old injuries, usually had a good deal of residual stiffness.

TABLE 6.—*Joint Dislocations*

Distal interphalangeal joint	12
Proximal interphalangeal joint	5
Metacarpophalangeal joint	6

Complications noted in the old injuries were nonunion, malunion, rotation, infection, adhesions of both flexor and extensor tendons, ankylosis of the joints, and causalgia (Table 7). The treatment is outlined in Table 8. Attempts were made to handle these fractures in the simplest way possible. For example, if a simple fracture could be

TABLE 7.—*Complications Encountered*

Nonunion
Malunion
Malrotation
Infection
Adhesions of tendons
Ankylosis of joints
Causalgia

reduced by merely flexing the involved digit over a curved metal splint, this was done. When indicated, traction was applied either in the soft tissues or in the bone. Only rarely was it felt necessary to do an open reduction on a simple fracture. Attempts were made to immobilize only the finger

TABLE 8.—*Types of Treatment*

Closed reduction	12
Open reduction	
Primary	67
Secondary	12
Traction	
Kirschner wires through bone or skin	17
Splinting	21
Universal metal splint	5
Capsulectomy	5
Tendolysis	25
Arthrodesis	8

involved. This was to prevent stiffness to the other digits. The universal metal splint was used to good advantage in severe crush injuries and in multiple fractures. We did not hesitate to use small Kirschner wires in the reduction of many of these fractures in open wounds. We see no untoward reaction to these wires, and they usually facilitate early motion of the uninjured fingers.

The majority of complications that were encountered were seen in those injuries that were seen late. Malunion and nonunion, with rotation of the distal fragments, were encountered all too often in these old fractures. These complications were treated by open reduction and insertion of Kirschner wires. If union was not complete, it was possible to refracture the injured area, rotate the fragments to normal position, and place small Kirschner wires. If union was complete, it was necessary to do an osteotomy. Once the osteotomy was completed, the fragments were rotated into position and maintained in that position by small Kirschner wires and allowed to heal. Some workers use small bone grafts with this type of reconstructive surgery, with excellent results.

Infection is still occasionally seen in spite of widespread use of antibiotics. In this series nine infections were seen both in the early and in the late cases. Two of these had frank osteomyelitis.

It is rather common for adhesions to appear about the flexor tendons at the site of the callus formation. A tendolysis on the flexor tendons usually results in good functional digits if the tendon has not been injured too severely. If marked scar formation is present, then, of course, it is better to do a tendon-grafting procedure.

Joint stiffness, especially about the metacarpophalangeal joint, was seen all too frequently, and even in patients in whom only one finger had been injured. Capsulectomies were necessary in these cases. Improvement was rather remarkable in capsulectomies performed about the metacar-

pophalangeal joint. However, in procedures performed on the proximal interphalangeal joint, results were rather discouraging.

When fingers were injured too severely, amputations had to be carried out. This was especially true where both the flexor and the extensor tendons had been injured, along with the blood and nerve supply to the digits themselves. Some digits, where severe atrophy had occurred and where joint stiffness was marked, with subsequent poor tendon function, were also amputated.

Several cases of severe causalgia were also encountered. In these cases treatment was with cervical sympathectomy, with some improvement.

1405 Kale Building (26) (Dr. Posch).

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DISCUSSION

DR. ELDEN E. WECKESSER, Cleveland: It is a pleasure to discuss this very important paper, which has been presented very clearly and which covers a series of cases that is truly impressive, and to see the fine results Dr. Zelenock and Dr. Posch have had in Detroit.

The authors have emphasized that the principles of good fracture treatment are applicable to the hand, as well as elsewhere in the body. However, certain special circumstances are present in the hand, as Dr. Zelenock has pointed out. First, the fine hand joints (and there are many of them) tend to stiffen rapidly when the hand is immobilized. Second, the good blood supply to the hand tends to lead to osteoporosis when the part is immobilized. Third, the fine motions of the hand, requiring dexterous work, are greatly interfered with in malrotations and malunions. For these reasons, we should immobilize the part as little as possible, and immobilize in the position of function whenever we can.

Next, it seems most important to me to recognize unstable fractures. In my experience it seems very wise to size up the fracture when you first see it; if it is a transverse fracture and one that will stay reduced when it is put back in place, conservative means are in order. However, if it is an oblique fracture, one should be careful, because such fractures are the ones, especially in the phalanges, that lead to trouble. They lead to rotation deformities, so that the fingers overlap and normal function of the hand is lost. They lead to shortening, so that the extensor tendons and flexor tendons do not work properly.

As time goes on, I am more and more inclined to do open operations on these oblique, unstable fractures in the phalanges, and I am pleased to note that Dr. Zelenock and Dr. Posch are inclined to do the same thing.

Placing the longitudinal Kirschner wires for the metacarpals is a very fine procedure. We have chosen to utilize the unique anatomy of the metacarpal bones in that we have four parallel struts running close along one another, and usually we use the wires transversely, pinning the broken bone into the adjacent normal bone. Of course, in multiple fractures it may not be possible to use this technique.

DR. JOHN L. BELL, Chicago: I certainly have enjoyed hearing this paper. Most of our experience in fractures of the hand concerns itself with multiple fractures, such as are seen with severe crushing injuries.

Whereas in the past we relied mostly on molding the hand over the universal splint, in the last five years we have also utilized small stainless-steel wires to help hold multiple fragments together,

and we do not hesitate to make fine drill holes with a Bunnell bone drill and insert fine stainless-steel wires into the fragments to hold them together. I think this has been an addition and has helped us maintain reduction in these severely comminuted fractures.

It is not possible to discuss all the phases of this paper. However, in reading it over, I have certainly agreed with almost everything the authors have said. We are not much inclined, however, to use skeletal traction in the management of multiple fractures. We have found that careful molding over the universal splint and the addition of internal fixation have worked out fairly well, and it is only in the rare case that we have had to resort to skeletal traction.

Observations on a New Anesthetic Agent, Fluothane

CHARLES B. PITTINGER, M.D.; STUART C. CULLEN, M.D., and DEAN C. WATLAND, M.D., Iowa City

Fluothane (2-bromo-2-chloro-1,1,1-trifluoroethane) is a potent, nonexplosive anesthetic agent recently developed by Imperial Chemical Industries of England. It is a volatile liquid having the chemical structure indicated in the Figure. Johnstone [1] published the first clinical report of its use in September, 1956; another, by Bryce-Smith and O'Brien,[2] appeared in December, 1956. In addition to the properties already mentioned, Fluothane was stated to possess a not unpleasant odor, which, in addition to its great potency, allowed for short, pleasant inductions, usually with little or no excitement. Excellent muscular relaxation, rapid recovery, and a low incidence of nausea and emesis were also reported. Although hypotension accompanied by bradycardia was said to occur, the impression gained from the available information was sufficiently encouraging to prompt an investigation of this new anesthetic agent.

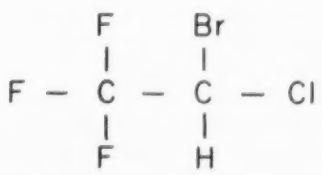
The purpose of this report is to present some clinical observations on the first 220 patients anesthetized with Fluothane in our hospitals. Their ages ranged from 4 weeks to 94 years. One group included the usual types of hospitalized patients scheduled for general surgical, urological, gynecological, orthopedic, thoracic, neurosurgical, otolaryngological, ophthalmological, and oral surgical procedures of from 10 minutes' to 5 hours' duration. Another group consisted of outpatients scheduled for minor procedures, mostly oral surgical in nature. No patients were excluded from the study because of age or debility. Both good- and poor-risk patients were included. Most anesthetics were administered by anesthesiology residents.

In view of the reported hypotensive effect of Fluothane, an analysis (Table) was made of blood pressure changes during anesthesia and surgery in the hospitalized patients. These patients were categorized according to the degree of muscular relaxation and depth of anesthesia usually considered necessary for the various procedures. During induction, the incidences of depression of blood pressure of less than 30 mm. Hg, in the range of 30-60 mm. Hg, and greater than 60 mm. Hg are indicated for each of the categories. The degree of hypotension during induction did not vary appreciably in the three categories.

Blood Pressure Changes During Fluothane Anesthesia in 148 Patients

	Induction, %			Maintenance, %		
Fall in Pressure, Mm. Hg	<30	30-60	>60	<30	30-60	>60
Relaxation required						
Pronounced	70	20	10	43	36	21
Moderate	85	13	2	93	4	3
None	78	14	8	71	26	3

However, during maintenance of anesthesia, there was a tendency toward a greater fall in blood pressure in the cate-



Structural formula of Fluothane (2-bromo-2-chloro-1,1,1-trifluoroethane).

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From the Division of Anesthesiology, Department of Surgery, State University of Iowa College of Medicine.

gory of patients requiring the most relaxation, as indicated by increases in percentages having falls of 30-60 mm. and greater than 60 mm. Hg, and a decrease in the precentage having falls of less than 30 mm. Hg pressure, as compared with the categories requiring only moderate or no relaxation.

In most of these patients it was possible to lighten anesthesia and allow a return of blood pressure toward normal without hindering the surgical procedure. Occasionally, other methods were necessary. Atropine intravenously was given when bradycardia accompanied the hypotension. As the bradycardia was corrected, the pressure usually rose. In other instances vasopressors were used to correct hypotensive episodes. There were no cases of severe, intractable hypotension encountered in this series.

A review of 47 cases requiring pronounced relaxation revealed that in only 4 was it necessary to use a muscle relaxant to facilitate the surgical procedure. A relaxant was used for the insertion of an endotracheal tube in only 5 of 83 patients who were intubated.

To a group of 37 outpatients anesthesia was administered for periods of 10 to 60 minutes, mostly for oral surgical procedures. No premedication was given except to a few who received atropine. No blood pressures were taken, but the peripheral pulse was followed closely throughout the procedure. Bradycardia was not a pronounced problem in these patients. Average induction time of anesthesia was four minutes. This was the period from the beginning of anesthesia to the beginning of surgery. Recovery time, which was considered to extend from the end of the surgical procedure to the moment the patient could answer questions coherently, was an average of four minutes. It was only an additional five minutes, on the average, until the patient was able to walk to a recovery room.

Since the latter group received no premedication, except occasionally atropine, and they had only minor surgical procedures, some of which required as long as an hour of anesthesia, it was considered a good group in which to study the occurrence of postanesthetic nausea and emesis. In only one case did emesis occur, and this followed the swallowing of a considerable quantity of blood by a 10-year-old girl who had several teeth extracted. When these patients were questioned concerning the anesthetic procedure, comments were uniformly favorable.

In the entire series, there were four postoperative deaths. No deaths occurred in the operating room. One death occurred 34 days postoperatively in a 40-year-old man with severe diabetes and progressive Kimmelstiel-Wilson disease and was due to an acute myocardial infarction. Another death occurred 44 days postoperatively in a 68-year-old woman who developed multiple biliary fistulae following an exploration of the common bile duct and who had a second surgical procedure with cyclopropane anesthesia for profuse bowel hemorrhage just three days before she died. A third death occurred three days postoperatively in a 79-year-old man who had a leg amputation and who had been in severe cardiac failure with bilateral pleural effusions and pulmonary edema preoperatively. The fourth was that of a 3-year-old hydrocephalic girl and occurred 34 hours after a five-hour procedure, consisting of ventriculograms and revision of a subarachnoid-ureteral shunt. She had a highly elevated cerebrospinal fluid pressure, exhibited cyanosis after 24 hours in spite of a clear airway, and 10 hours later become apneic and died.

Observations in our preliminary experience with Fluothane concur with those reported by the British clinicians. Hypotension during anesthesia with this agent does not appear to be sufficiently severe to limit the general use of the drug, which possesses many desirable features. On the basis of

our impression that Fluothane is a very promising anesthetic agent, a research program including clinical and laboratory studies is in progress. Potentiation of the neuromuscular effect of tubocurarine chloride U. S. P. by Fluothane has been ascertained in rabbits using the sciatic nerve-gastrocnemius muscle preparation. The action of the drug upon isolated mammalian heart is being studied. Cardiovascular and respiratory effects of the anesthetic agent are being investigated in dogs and human beings. Some electroencephalograms have been recorded during Fluothane anesthesia, and a method for determining the agent in blood is being developed in order to correlate, if possible, electroencephalographic patterns with blood and clinical levels. Investigations of the effects of the drug upon hepatic and renal function are being designed.

Imperial Chemical Industries, the manufacturer, and Ayerst Laboratories, the distributor, supplied the Fluothane which has made possible our investigations.

University Hospitals.

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DISCUSSION

Dr. Charles B. Pittinger, Iowa City: Dr. Watland has presented the evidence for our continued interest in Fluothane. Up to the present time we have anesthetized over 300 patients for surgical procedures. The response of the anesthesia staff has been enthusiastic. We have met with no opposition from the surgical staff, and actually have been encouraged in the use of Fluothane by favorable comments from some of them.

Fluothane anesthesia at the present time is new. Drug evaluation, of course, is a long, drawn-out procedure, requiring much time; and Fluothane has only reached the stage of initial clinical trial, its use having started in this country a few months ago. For that reason, much more research is necessary, particularly along the line of toxicological investigations.

Dr. Watland has mentioned the renal and hepatic function tests which we expect to get under way shortly in a series of patients. These tests are indicated because of the chemical relationship of Fluothane and chloroform. In the 300 or more anesthetic procedures with Fluothane, there has been observed no evidence of hepatic or renal toxicity.

The matter of hypotension, as Dr. Watland has pointed out, is not a serious limiting factor. In most instances satisfactory anesthesia with Fluothane is possible without severe hypotension. In the few instances in which it was considered advisable to increase blood pressure during anesthesia, response to vasopressors or atropine was satisfactory.

Dr. Robert T. Tidrick, Iowa City: I do not believe surgeons should talk too much about this subject. I think the anesthesiologists should have pretty free rein. Of course, the surgeon is interested in whether his patient stays alive and seems to be relaxed, but when we are associated with colleagues like Dr. Pittinger, who is a pharmacologist too, we have to listen to the experts. So far, we have been very pleased with this agent.

Criteria for Satisfactory Colectomy for Carcinoma of the Left Colon

Description of Early High Ligation of the Inferior Mesenteric Vein

STANLEY R. FRIESEN, M.D., Kansas City, Kan.

With the almost universal adoption of "left colectomy" rather than segmental resections of carcinomas of the sigmoid and left colon there is still some discrepancy in the type of operation advocated. Diversity of techniques of the component parts of a "left colectomy" results in disagreement as to what constitutes an adequate resection and leads to difficulties in the evaluation of the results of surgical treatment. As compared with resections of the right colon, there is no standardized left colectomy.

An adequate and satisfactory resection for carcinoma of the colon should have for its purpose (1) the wide removal of the primary lesion in continuity with appropriate tissue pathways (venous and lymphatic) of potential secondary spread compatible with minimal morbidity and mortality; (2) the prevention of spread occurring as embolization or "seeding" during operation; (3) the recognition and removal of precursors of potential new growths, and (4) the salvage of as many patients as possible as measured in long-term survivals, free of cancer. Furthermore, a plan of operation for carcinoma of the colon should be based on principles soundly established by Halsted for the radical excision of carcinoma of the breast.[1] It is accepted as standard procedure in the radical mastectomy of Halsted that the venous drainage (branches of the axillary vein) be interrupted prior to the lymphatic dissection of the axilla, and before the final amputation of the breast.

Interesting reports concerning mode of spread and means and sites of recurrence should influence the adoption of pertinent techniques. It has been reported by Fisher and Turnbull[2] that tumor cells were recovered by a perfusion technique from the blood of the major mesenteric venous channels in 8 of 25 cases (32%) of colorectal carcinoma. This incidence is in agreement with that of Grinnell,[3] who reported a 33% incidence of vein invasion as found by microscopic study. Barringer et al.[4] utilized a radiological technique in the study of the venous bed of resected specimens of colon carcinomas and found that 51% of 45 specimens demonstrated vessels occluded, presumably, by tumor. Cole and associates[5] have advocated early ligation of the blood vessels in colon resection before any manipulation of the tumor, incident to its resection, is begun. Such a precaution is advocated for the prevention of extrusion of bits of tumor as emboli into the liver and other organs. Cole[6] has also called attention to the danger of implantation of tumor cells in the anastomotic suture line by means of the suture carrying malignant cells, which may have broken off from the tumor, from the lumen of the bowel into the bowel wall. To prevent recurrences at the anastomotic line, Cole advocates preliminary ligation of the bowel itself several inches proximal and distal to the tumor. Recurrence at the anastomotic line may also occur, of course, if section of the bowel has been made too close to the lesion. However, spread of

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From the Departments of Surgery and Pathology and Oncology, University of Kansas School of Medicine.

colonic cancer seldom extends far along the wall of the colon and lymphatic spread distal to the tumor usually does not extend beyond 5 cm. Gilchrist and David[7] reported that lymphatic spread was found 1 to 5 cm. distal to the tumor in only 4.6% of their cases.

"Recurrence" of cancer in the colon wall may in reality represent a new carcinoma or one originating in a polyp of the colonic mucosa overlooked at the time of resection. The incidence of associated polyps of the colon in known cases of carcinoma of the colon was reported to be 38% of cases studied by Lillehei and Wangensteen.[8] Because of this high incidence of associated precursors of cancer, they advocated total or near-total colectomy for carcinoma of the left colon. They stated that the preservation of the pelvic colon, the terminal ileum, and the cecum is sufficient usually to prevent diarrhea and alimentary crippling.

Recurrence of colonic cancer, however, is more likely to occur as a result of lymphatic spread than as recurrence in the bowel wall. This is evidence by reports of the sites of residual tumor noted at the time of "second-look" operations.[9] The commoner sites of recurrence or continuing tumor growth have been shown to be along the para-aortic lymphatics, as well as the lymphatics along the iliac vessels. This information supports Wangensteen's suggestion that a more complete removal of central lymphatics along the major vessels at the time of the original colon resection is indicated.

Keeping in mind the stated objectives of operation for carcinoma of the colon, the basic precepts of Halsted, and the observations of others concerning sites of recurrence and modes of spread, a plan of operation embodying the theoretically and practically desirable features of colectomy for carcinoma of the left colon is suggested.

The Operation

Although it is necessary to gain exposure of the peritoneal cavity from the retroperitoneal duodenum to the sacral hollow, a difficult part of a left colectomy is the freeing-up of the splenic flexure of the colon. For this reason, as well as the anatomical, physiological, technical, and cosmetic advantages of transverse incisions, an incision beginning near the left flank and extending across the abdomen, medially and inferiorly to 3 to 4 cm. beyond the midline, is recommended (Fig. 1). The incision allows ready access to the splenic flexure, as well as the retroperitoneal space from duodenum to rectum. If it becomes necessary to remove the right colon as well, the incision is easily extended to the right.

After the incision has been made, abdominal exploration is done to determine specificially the presence or absence of metastases, lymphatic and hepatic, and the resectability of the primary lesion. With few exceptions, resectability can be determined with only minimal and brief manipulation of the tumor. If hepatic metastases are present and the primary

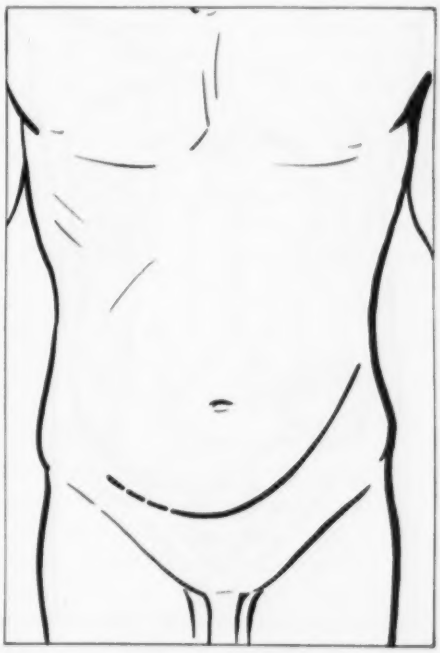

Fig. 1.—Diagrammatic illustration of an abdominal incision for the performance of colectomy for carcinoma of the left colon and rectosigmoid.

lesion is resectable, one may properly elect to carry out a limited or segmental resection; however, if hepatic metastases are not palpable, a planned extended resection, such as is described here, is indicated.

Without further manipulation of the tumor or surrounding tissues, the first definitive procedure of the resection is for the purpose of immediate ligation of the inferior mesenteric vein to block any embolization of tumor cells to the liver due to later handling of the primary carcinoma. The isolation of the inferior mesenteric vein at its junction with the splenic vein is simply accomplished by the expedient of first elevating the most proximal segment of jejunum and dividing the ligament of Treitz (Fig. 2). The vein comes clearly into view by this technique and does not require extensive retromesenteric dissection or division of the lateral peritoneal reflections. After the inferior mesenteric vein has been ligated and divided at the splenic vein, one may wish to apply circumferential tapes around the colon on either side of the primary tumor, as advocated by Cole, to prevent luminal migration of tumor cells. Manipulation of the tumor itself is still avoided. In accordance with the tenets of Halsted, the lymphatic dissection is then carried out. The retroperitoneal duodenum, exposed by the division of the ligament of Treitz, is elevated, and the lymphatic and areolar tissue over the anterior and lateral surfaces of the aorta and vena cava is grasped lightly and dissected from them, beginning from under the duodenum and pancreas and progressing inferiorly. A small anterior artery from the aorta is occasionally present and is ligated before the larger inferior mesenteric artery is seen. The latter artery is cleansed, doubly ligated at the aorta, and divided. The posterior peritoneum is further incised, and the paraaortic and caval dissection is carried inferiorly to and beyond the bifurcation, into the sacral hollow, and along the iliac vessels bilaterally. During this dissection the ureters are isolated, and all loose retroperitoneal tissues between them are contained in the lymphatic block of tissue. The ovarian vessels in the female patient may or may not be spared, as indicated in individualized cases. The lymphatics at the bifurcation of the common iliac arteries should be included in the excision. The lymphatic dissection should extend inferiorly to a point at least 5 cm. or more distal to the most caudal margin of the tumor and to the site of election of division of the distal bowel.

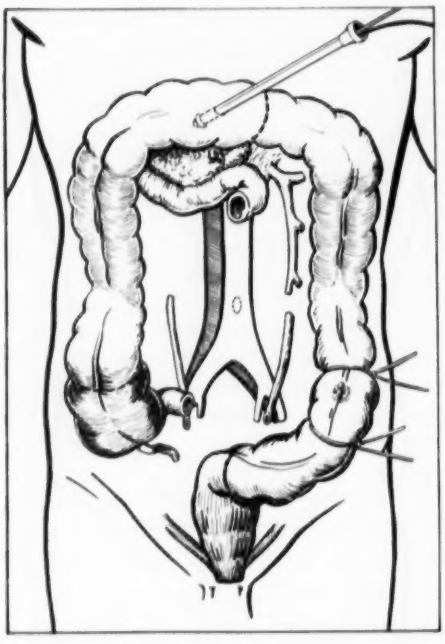

Fig. 2.—Diagrammatic illustration of the composite features of colectomy for carcinoma of the left colon. (See text for description of steps in technique and rationale of procedure.)

At this time the transverse mesocolon is elevated and transilluminated for identification of the middle colic vessels. The mesentery just to the left of the midcolic vessels is incised from the transverse colon to the ligated inferior mesenteric vein, completing the division of the entire left colic mesentery. The transverse colon is divided with cautery between clamps, with an anastomotic clamp on the proximal side, just to the left of the midcolic vessels.

The proximal portion of the bowel can be used either for a subsequent anastomosis or a terminal colostomy in the event the rectum is to be excised as well. The left omentum is then divided at the gastro-epiploic vessels, and the lateral peritoneal reflections are divided. The splenic flexure is freed up either from above or from the descending colon, care being taken not to injure the splenic capsule.

The peritoneum at the level of the primary lesion is incised widely and the carcinoma mobilized. At this time a final decision as to whether the operation is to be an anterior resection or a combined abdominoperineal excision must be made. This decision, of course, depends primarily upon the level and location of the primary lesion. In addition, some consideration should be given to the circumstances relating to cure or palliation. If hepatic metastases are present, for instance, every effort should be made to preserve the lower rectum and anal sphincters; if lateral spread and adjacent visceral involvement are present, complete excision of the rectum is advisable. The predominant factor, however, affecting the choice of operation at this point is usually the level of the lesion. If the carcinoma is situated where lateral and distal lymphatic spread is likely to involve the levator ani muscles, a complete excision of the rectum, anus, and levator ani is mandatory. If, on the other hand, that level of the bowel at least 5 cm. distal to the most inferior margin of the tumor is well above the levator ani muscles and their lymphatics, anterior resection is indicated if technically feasible in the individual case.

The level of the peritoneal reflection on the distal bowel is extremely variable in individual cases, extending from the lower sigmoid, in some patients, to the low rectum, in others. Because of this variation it would seem that the location of the lesion in relation to the peritoneal reflection would not be as logical a criterion for selection of operation as would the location of the lesion in relation to the lateral lymphatic spread along the levator ani. Reperitonealization of the pelvis is usually possible in any instance.

If an anterior resection and anastomosis is selected for the carcinoma which is sufficiently above the area of lateral lymphatic spread, certain theoretical precautions can now be taken to avoid the possibility of anastomotic "seeding" or implantation. The bowel is divided well distal to the lesion between clamps, with the anastomotic clamp on the distal side. Cautery is used for this not only for the usual advantages of hemostasis and relative asepsis but also for the purpose of destroying the possible cells in the lumen which may have been trapped at the site of division of the bowel.

The specimen, left colon and mesentery, is given to the pathologist. Before the anastomosis is begun, the surgeon must ascertain whether polyps or a second small carcinoma may be present in the right colon. To assist him in this inspection, the pathologist should open the resected left colon to determine whether additional polyps are present, noting their location if present. The surgeon, after careful palpation of the right colon, may insert a sigmoidoscope into the lumen of the right colon and, by reefing the colon on the instrument, inspect the entire right colon. If polyps are present, it is advisable to resect the right colon to the level of the cecum, as advocated by Wangensteen, for anastomosis of the cecum to the distal portion of the bowel or rectum. The latter procedure of near-total colectomy has an additional advantage over left colectomy in that the follow-up of the patient need involve only repeated sigmoidoscopic procedures, without repeated barium enemas.

The anastomosis is made end-to-end, utilizing closed anastomosis clamps. As mentioned above, the use of coagulating cautery obviates the need for a hemostatic mucosal suture layer. A one-row anastomosis is made, using interrupted 0000 oiled nonabsorbable surgical (silk) sutures, which

ideally traverse the seromuscular layers, avoiding the lumen of the bowel and avoiding, theoretically, the potential implantation of tumor cells in the suture line. The inverted tissue which was held and coagulated in the anastomosis clamps becomes necrotic and sloughs into the lumen. There has been no evidence of tension on the anastomotic suture line when the transverse colon has been joined to the rectum. Anastomosis of the descending colon to the rectum without release of the splenic flexure is likely to be attended by undue tension. The retroperitoneal space is reperitonealized by suture of the right mesocolon to the ligament of Treitz and the posterior peritoneum. The lateral peritoneal reflection is sutured to the fatty tags of the colon. The abdomen is closed without drainage with interrupted sutures of stainless steel wire in the fascia and 0000 silk in the skin.

Postoperative Management

When it is felt that microscopic tumor embolization or implantation may have occurred prior to or during operation, a course of intravenous sterile mechlorethamine hydrochloride N. F. (nitrogen mustard) therapy is begun on the day of operation, as has been suggested by Cruz, McDonald, and Cole.[10] Repeated follow-up visits include sigmoidoscopy every six months and radiological examination by barium enema every year. The practice of carrying out "second-look" procedures from six to nine months following operation in selected cases offers a real opportunity for the early removal of recurrence or residual tumor. In a limited personal experience, two patients already have been converted from a cancer-positive to a cancer-free status by means of reexploration, at which time redissection of the retroperitoneal tissues was done.

Although the operative procedure described above has been used personally for five years, insufficient elapsed time and number of patients preclude accurate documentation of the expected increase in incidence of survival.

Summary

A technique of operation for an adequate resection of carcinoma of the left colon is described. In cognizance of the possibility of embolic and lymphatic spread, the plan of operation emphasizes the avoidance of manipulation of the primary tumor; a simple approach to early high ligation of the inferior mesenteric vein; the early paraaortic and retroperitoneal removal of higher echelons of lymph nodes; the ligation of the inferior mesenteric artery at the aorta; the aim of prevention of recurrence through "seeding" by the utilization of tapes, cautery coagulation, and nonmucosal sutures, and the search for, by right coloscopy, and the removal of all precursors of carcinoma of the colon.

Greater emphasis upon the adequate excision of tissues at the expected sites of recurrence, the prophylaxis of tumor embolization and implantation, and the precepts of Halsted in cancer surgery should lead to a greater measure of salvage of patients with carcinoma of the colon.

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DISCUSSION

DR. WARREN H. COLE, Chicago: I believe Dr. Friesen has outlined a splendid operative plan to minimize the possibilities of implantation and venous emboli. I personally believe that if we can adopt the principles of this type, we shall definitely minimize these recurrent phenomena, which show up so often.

I am delighted to see his technique for ligation of the inferior mesenteric vein, because that vessel carries a tremendous venous load, and one would think that the cells would get loose there into the portal system in large numbers unless one ligated the vein early in the operation, as he described.

For years I have been worried about venous emboli, and in our studies in 1953 we found cancer cells in the blood from veins draining from the tumor by perfusion. That work was added to very much by the splendid report and work of Fisher and Turnbull, which Dr. Friesen has already referred to.

I think the most dramatic article on this subject is the recent one by Engel, of Copenhagen. For example, of 65 patients with operable tumors he found cancer cells in the systemic blood (from the antecubital vein) in 3. Of 14 patients with advanced cancer he found cancer cells in the systemic veins in half. When he examined blood from the vein draining the tumor, there was a higher incidence, as one would expect. For example, he reported cancer cells in 35% of patients having Grade 2 tumors, 78% in patients with Grade 3 tumors, and 100% in patients with Grade 4 tumors.

There is no proof, of course, that these emboli will grow and produce metastases; in fact, Engel states in his conclusions that he cannot prove that these grow and produce new metastases. He stated that his three-year survival figures did not seem to indicate that it made much difference whether these cells were present in the venous blood or not. I should like to call your attention to one very important fact that I suspect he may be minimizing, namely, that it is the venous emboli that kill the patient; there cannot be bone metastases or lung metastases unless there are venous emboli.

I believe we must do our best to prevent these venous emboli, because theoretically if we can prevent them we shall prevent metastases except those derived from lymphatic deposits, which I believe give rise to the venous spread comparatively late.

DR. CAMPBELL GARDNER, Montreal, Canada: This is an excellent presentation, but I differ from, or rather question, many of the points suggested.

Speaking of Dr. Halsted, if my memory serves me well, he did perform a very radical type of operation for carcinoma of the breast at one stage of his brilliant career, even going so far as to divide the clavicle, removing the axillary vein and dissecting out all of the nodes in the supraclavicular region. Later, as I remember, he decided that this heroic procedure did not improve his results, and he therefore abandoned it. Recently, in Montreal, Dr. Huggins, of Chicago, offered the hypothesis that every malignant tumor has a life period unto itself. He did not try to prove this point, but it would seem one that should be considered.

I cannot see that Dr. Friesen has proved that the emboli present in the blood stream were not already there. If he believes that the whole inferior mesenteric vein should be removed, why then not carry the procedure still further and remove the splenic vein at least to the point where it enters the portal vein, if not farther?

As far as the length of bowel to be removed is concerned, there would seem to be no particular reason why one should not excise the whole of the colon, and even part of the small intestine as well, if one so desired.

I regret that I am not convinced, or even impressed by the criteria so far expressed, as to just where removal of those tissues adjacent to a carcinoma should stop. I suppose it depends upon one's philosophy, therefore either one is content with the removal of a reasonable amount of bowel, with its lymphatic drainage, or one could carry the procedure almost *ad absurdum*.

By and large, I am content to ligate the inferior mesenteric artery and vein as close to the origin of the artery as possible, and whether or not I have resected all the cancer or whether it has already passed beyond this point, either by lymphatic or by venous drainage, is a matter of

chance, and I doubt (though I am prepared to be convinced) that a more radical operation would improve the prognosis.

DR. MAX M. ZINNINGER, Cincinnati: There are two sides to this question. Dr. Cole and his associates have indicated the importance of ligating the bowel on each side of the tumor to prevent implants. That is a very important consideration. I believe that using the cautery, as advocated by the essayist, is also important in preventing local recurrences, because it forms a local area in which implants are not likely to occur. It is an area that is going to slough out. It is not a suitable place for implants to occur.

I am inclined to agree with Dr. Gardner, of Montreal, regarding the method of such high ligation of vessels and extensive dissection. Perhaps I am a little inclined to be fatalistic, but I believe, as he does, that one is likely to cure the patient by more conservative resection in the vast majority of cases; and if such extensive resections are done routinely, I question whether the mortality rate will not rise and the end-results be very little improved, if improved at all. For that reason, I am continuing to carry out the same type of resection that I have been doing for 25 or 30 years. If the tumor emboli are present in the blood before one starts to operate, I don't see how one is going to prevent them from going farther by making a high ligation of the vein. Perhaps a lower ligation, nearer the tumor of a a tributary of the larger vein, may be just as efficacious.

The recurrence rate in patients with carcinoma of the colon is not nearly as high as it is in many other types of cancer. We cure many such patients with the more moderate types of resection that many of us have been carrying out for years.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: Dr. Ransom, where do you ligate the vessels?

DR. HENRY K. RANSOM, Ann Arbor, Mich.: In Ann Arbor we feel very much as does Dr. Zinninger. If one performs right colectomy for cancer of the cecum, it would seem logical to perform left colectomy for cancer of the sigmoid. However, the problem is not exactly the same, and one wonders whether left colectomy with reconstruction by anastomosis of the transverse colon to the rectum, if used routinely, would not result in a higher operative mortality than would be justifiable in order to remove a few additional nodes which possibly might be involved. Although size and hardness of lymph nodes are not entirely reliable criteria of cancerous involvement, none the less extensive involvement is unmistakable grossly. Thus, in cancer of the sigmoid or rectum, if the nodes along the superior rectal or sigmoidal arteries appear to be involved, ligation of the inferior mesenteric artery at its origin is performed. When there is no gross involvement of nodes in this area, a more distal ligation is usually performed.

A few years ago Dr. Vernon Astler (Astler, V. B., and Coller, F. A.: Prognostic Significance of Direct Extension of Carcinoma of the Colon and Rectum, *Ann. Surg.* 139:846, 1954), working in our pathology laboratory, studied a number of surgical specimens of cancer of the colon and rectum by the use of large sections especially prepared. These large sections included the entire circumference of the bowel and could be examined both grossly and microscopically. Spread of cancer by direct extension was possible with these "life-size" sections. In general, it was observed that penetration by cancer of all coats of the bowel, with extension into the adjacent adipose or connective tissue, had occurred at the time of resection in about 80% of cases. Forty per cent revealed positive lymph nodes. This study emphasized the importance of spread of cancer by direct extension and a progressive decline in survival rate proportional to the depth of penetration of the colonic wall.

DR. R. KENNEDY GILCHRIST, Chicago: This discussion could go on all day. First, I should like to say something about the mucosal stitch, Dr. Friesen, because I use it all the time. Fortunately, it has not been my experience to have suture-line recurrences except in very advanced cancer. I believe that this is due primarily to our never using the sponge a second time. I think that one of the reasons many people get so many implants is that they keep reusing a sponge and implanting cells into the suture line.

Dr. Friesen's scheme of cautery, which is something like Fred Rankin's, may well prevent implantation, since the mucosal edge dies and sloughs, but it is interesting how many of us who do a fair amount of bowel surgery do not seem to be plagued by suture-line recurrences. We certainly have our recurrence rate otherwise. I might give you just a few figures from memory; they are approximate.

In a study we made a good many years ago, if we had reported our figures the way most people do, forgetting all those patients who died in the hospital, who were run over by trains, who had coronary occlusions, or who were lost to follow-up, but who had cancer of the sigmoid, none of whom had the inferior mesenteric artery removed, none of whom, as far as I can remember, had any ligation proximal to the left colic artery, 90% of those who had no nodes involved were known to be free of cancer five years. This includes every patient who went on the table and in whom the surgeon thought he had any chance of cure. Of those who had nodes involved in the same position, the figure was 75%.

Of those with cancer below the peritoneal reflection, almost 50% with node involvement were free of cancer five years—again, if you threw out all the others and kept nothing but the so-called adjusted statistics, i.e., you threw out all the patients who didn't have a chance to live five years. In those who did not have any nodes involved it was 88%.

I do not always remove the inferior mesenteric artery. I do so in lesions above the sigmoid, in a fair share of cases, but it depends somewhat on the lesion. It has been my experience that one can pretty well guess as to lymphatic metastasis. Vascular metastasis is something different. Certainly, when the lesion is below the peritoneal reflection, I see no reason for taking out the inferior mesenteric artery for cure, for if there are nodes involved to the aorta they are certainly involved along the hypogastric arteries and laterally. That extension plays a significant role.

This operation is a beautifully designed one, and I do think we ought to look for polyps, as has been done here; but I am not so sure that we always need to make as extensive a resection.

I point out only one thing further, as noted by Willis, who wrote an excellent textbook many years ago, recently revised, called "The Spread of Tumors in the Human Body," in which he pointed out that vascular metastases do not survive unless the field is right, whatever the body resistance may be, and, second, that they must all attain a new blood supply, even though they may be in any vascular structure you might wish to name—that they float there, they may live there for quite a long time, but they must get a new blood supply before they will live.

I believe that is the crux of a great deal of this problem, namely, what the host resistance really is. That is what Dr. Gardner was talking about.

I think all these other steps are in order.

DR. CLAUDE J. HUNT, Kansas City, Mo.: Dr. Friesen has presented an excellent paper advocating an extensive excision of the left colon for all malignant lesions regardless of the apparent extent of spread. He has done an extensive amount of colon surgery and is an outstanding young surgeon in our community. I therefore am glad to commend him on his heroic approach, at the same time stating we believe that the extent of the operation is related to the condition found on exploration. I cannot believe it is necessary to do an extensive complete left colectomy for an apparently localized annular carcinoma of the sigmoid or descending colon. The local condition and evidence of extension are of the greatest importance in determining the extent of resection for lesions of the left colon. The situation is not comparable to a right colon lesion. Complete left colectomy is far more extensive than right colectomy, is attended by more bowel removal, greater technical difficulty in bowel restoration, and more possibility of bowel tension or vascular deficiency.

It is true that no one would attempt to do a segmental resection of a portion of the ascending colon. An extensive resection of the entire ascending and the proximal portion of the transverse colon, along with a segment of the terminal ileum, is the accepted procedure for malignant lesions of the right colon. On the left, however, the colon is longer, and the blood supply is such that to ligate the inferior mesenteric artery and vein at their point of origin or junction requires a considerable compromise of bowel for an annular lesion that presents no evidence that extension, glandular or venous, has proceeded to the point where such a radical approach should be followed. Cure in such instances is not to be expected regardless of the extent of the resection, although the procedure is often justified for palliative relief.

Each case should be individualized, and the extent of surgery determined by the extent of fixation and glandular extension. Invasion of the venous system is comparable to invasion of the middle thyroid vein in thyroid surgery. When malignant implants are present, systemic dissemination has most likely occurred, and, regardless of the radicality of the procedure, the patient will not be cured. We try to evaluate the extent of the malignancy and adjust the surgery accordingly. Most usually it is an extended segmental resection with wide mesenteric extirpation. We believe vessel ligation and tumor isolation by bowel ligation above and below the lesion should precede mobilization of the segment of bowel to be resected. Complete left colectomy with end-to-end anastomosis can only be done when there has been no previous fixation of the right colon to the abdominal wall in the nature of a colostomy. This introduces the controversial subject of colostomy versus cecostomy in the decompression of the acutely obstructed colon from a left colon lesion. We have for many years and upon numerous occasions advocated cecostomy rather than right-colon colostomy. We have, however, condemned the usual type of purse-string catheter cecostomy but have insisted upon the stoma's being a surface one, as in colostomy. A surface cecostomy stoma affords an adequate opening for bowel irrigation, and by the use of the clamp we devised several years ago, a cecostomy can be largely aseptically performed. This is truly a cecal stoma on the surface of the abdomen, as is a colon stoma. It is adequate for bowel irrigation and bowel preparation for subsequent surgery and in no way restricts the extent of subsequent surgery on the left colon. With a cecostomy the vascular status of the cecum can be determined; this cannot be determined when a right colostomy is done. It is at this site that vascular deficiency will occur in

protracted acute distention of an obstructed left colon. There is much in favor of a surface cecostomy when a surgical decompression is necessary that is not present in a right colostomy.

This subject is a timely one, and frequently discussed. It has been well presented by Dr. Friesen, and his points have been ably discussed.

DR. WARREN H. COLE, Chicago: It has been very interesting and amusing to hear this discussion. It is a controversial subject, and we can prove very little to date.

We have to realize that cancer cells kill and we should exert all possible effort to kill them whenever possible. I believe we also must appreciate that if we handle a tumor rather roughly we are going to dislocate cells, which will then get loose and drift into veins, lymphatics, etc.

The data that Turnbull has obtained, as well as ours, indicate that if we handle the tumor, we dislocate cells, which will drift into the veins, lymphatics, and elsewhere. It is my contention that, although various chemicals, such as mechlorethamine and triethylenethiophosphoramide (Thio-TEPA), are of comparatively little value in the treatment of advanced cancer, these chemicals would be effective against cells that are loose and do not yet have a vascular attachment.

We can prove this in animals. When we inject a suspension of Walker 256 cells into the portal vein of rats, "takes" are produced in the liver in 85% to 90% of animals. If we give mechlorethamide within an hour after inoculation, the "takes" are reduced to 10% or 20%; if the mechlorethamide is given 48 hours after inoculation of cells, the "takes" are reduced in the treated animals by only 10% to 15% less than in the controls. In animals, anticancer agents can kill loose cells, although they may not kill them after they are attached and have developed a blood supply. We presume anticancer agents might have the same effect in humans.

If cells are desquamated into the wound, peritoneal cavity, and veins during operation, and we can destroy at least a large part of them, we should certainly be helping the patient in his fight against them. It now appears that only a small proportion of cells found in the veins and elsewhere actually live. In animals, 5000 cells of a certain tumor may not produce a "take" of the tumor, but 50,000 cells will.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: Do you give your drug at the time you remove the colon, or afterward; and what do you give?

WARREN H. COLE, Chicago: For the past year we have been giving mechlorethamine hydrochloride at the time of operation (e.g., resection of the colon for cancer), putting it into the abdominal cavity or injecting part of it into a tributary of the portal vein. We are giving it in doses of 0.1 mg. per kilogram, with a maximum dose of 7.5 mg. on the day of operation. We then give the same dose intravenously each day for the next three days.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: The same dose—7.5 mg.?

DR. WARREN H. COLE, Chicago: Yes. We have used that as our maximum, because I think fat people will not tolerate the drug as well. They appear to be susceptible to wound infections after injection of mechlorethamine because of hematopoietic depression.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: How about age? Does age make any difference?

DR. WARREN H. COLE, Chicago: To date we have limited the therapy to patients 70 years of age or less.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: And you are still using mechlorethamine?

DR. WARREN H. COLE, Chicago: That's right. I might add that in about 34 cases in which we have used it intraperitoneally, we have lost 1 case, a rectal case. However, this patient received only one dose, namely, the one on the day of operation, because within 24 hours he developed a severe diarrhea, which was found to be a staphylococcal enteritis. I don't believe that the single dose of mechlorethamine killed that patient. I believe death was related to preoperative antibiotic therapy which the patient had received. We had another patient the other day in whom respiratory arrest and vascular collapse occurred at the end of the operation. We gave that patient 0.1 mg. of mechlorethamine hydrochloride intraperitoneally as the wound was closed. I don't believe that the mechlorethamine had anything to do with the respiratory complication; the arrest may have been related to a rather large amount of succinylcholine given during the operation to improve relaxation. However, I would warn you that the mechlorethamine is a toxic agent, and it is more toxic in patients who have recently been operated on, for two reasons: (1) It is a bone-marrow depressant, usually giving rise to a leukopenia, with perhaps an increased susceptibility to infection, and (2) there is a tendency for the wounds to bleed more than usual. However, we have had no serious postoperative bleeding.

DR. CAMPBELL GARDNER, Montreal, Canada: I would like to ask the speaker two questions: Since he believes that he should remove the inferior mesenteric vein to its termination, does he apply the same practice to the breast and remove the axillary or subclavian vein above the level of the clavicle? Second, would it be too much to ask his cure rate as compared with the cure rate of those of us who are carrying out the procedure generally used?

DR. STANLEY R. FRIESEN, Kansas City, Kan.: If I have done nothing more today, I have prompted a very interesting discussion.

I really don't know where to start. I take this criticism and discussion with good heart because I believe it has been given with the welfare of the patient in mind.

Before I answer Dr. Gardner's questions, I would agree with him that it is difficult to understand the growth of cancer. If we really understood this, operations in themselves probably would not be necessary.

As you probably know, Halsted described several operations for cancer of the breast. To make sure of this point I reviewed some of his articles on cancer of the breast just a few days ago, and the one I am talking about is precisely one of ligating the branches of the axillary vein, then the lymphatic dissection, and, finally amputation of the breast. It is true that he did manipulate the breast to some extent and removed it about half of the way before he went to the axillary part of the dissection. The rest of the operation is quite similar to what we do today—one of his operations, I should say.

Concerning the matter of segmental resection versus left colectomy, I would ask those who practice segmental resections for carcinoma of the colon whether they practice simple mastectomy or radical mastectomy for carcinoma of the breast.

I wish I had five-year survival figures with the utilization of this operation, but I don't. Although I have been doing an operation similar to this operation for five years, the number of patients and the length of time are insufficient to give you meaningful figures. However, from experience with patients who have operations similar to the one I have described, I am convinced that a left colectomy with wide excision of lymphatics offers a greater chance of survival than does a segmental resection. There are certain patients alive and free of cancer because of wider excision of lymphatic metastases which would have been missed with smaller resections. Perhaps at a later meeting I shall be able to back up this statement with follow-up figures.

I am very grateful for all of your discussions, particularly that by Dr. Cole, for I consider Dr. Cole a great preceptor in the fight against carcinoma of the colon. I ask merely to be a monitor of his teachings.

Relationship of Chronic Anorectal Disease to Carcinoma

JOSEPH A. BUCKWALTER, M.D., and MICHEL N. JURAYJ, M.D., Iowa City

An abundance of articles has been published concerning the clinical and pathologic aspects of epidermoid carcinoma of the anorectal canal. An occasional article refers to the possible role of benign anorectal disease in the etiology of this lesion. Cattell and Williams[7] discussed this possibility but reported a history of antecedent benign disease in only 1 of their 10 cases. Buie and Brust[6] found a history of local disease in 34 of 51 patients. Bensaude and associates,[3] Rosser,[12-14] Keyes,[11] Kerr,[10] Gabriel,[8] Bacon and associates,[2] and Grodsky[9] have mentioned the possibility but have not presented convincing evidence to support an association between previous benign disease and epidermoid carcinoma of the anus or rectum.

The more frequent reference to the possibility of such an association in earlier than in later articles suggests that this possibility and its clinical implications are not widely appreciated today. Practically all current surgery, pathology, and surgical pathology texts and monographs on proctology fail to mention the possibility that benign anorectal disease plays a role in the genesis of epidermoid carcinoma of the anus or rectum. In a recent discussion of the complications of anorectal surgery, the authors do not mention carcinoma as a possible sequela of improper, inadequate, or no treatment.[1]

Our purpose has been to assess the importance of benign anorectal disease in the genesis of epidermoid carcinoma of the anorectal canal. The clinical material consisted of 51 patients with this diagnosis seen at the University of Iowa Hospitals during the past 20 years. The data were obtained by review of the case records, from the tumor registry, and by correspondence with surviving patients and referring physicians. The results were examined for statistical significance by the χ^2 method of analysis; only the results of the analyses which were statistically significant will be reported.

Results

Thirty-one of the fifty-one patients, or just over 60%, had a definite history of benign anorectal disease existing before the diagnosis of epidermoid carcinoma of the anus or rectum. As Figure 1 shows, 18, or 75%, of the 24 men had a history of previous benign disease, as compared with 13, or slightly more than 48%, of the 27 women. This difference between the sexes is statistically significant at the 5% level when examined by the χ^2 method of analysis. The mean age of the 51 patients was 57.5 years; the age by sex is recorded in figure 1. One may observe the more than three-year difference in the mean ages of the two sexes.

In the report of findings and in the discussion, the 51 patients will be divided in most instances into those with and those without a history of previous benign anorectal disease. Figure 2 indicates the

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From the Department of Surgery, State University of Iowa College of Medicine.

Read at the 14th Annual Meeting of the Central Surgical Association, Chicago, Feb. 21, 1957.

Richard Shropshire, M.D., Washington, D. C., assisted in the collection of the data. Lloyd A. Knowler, Ph.D., Chairman of the Department of Mathematics and Astronomy, State University of Iowa, examined the data for statistical significance.

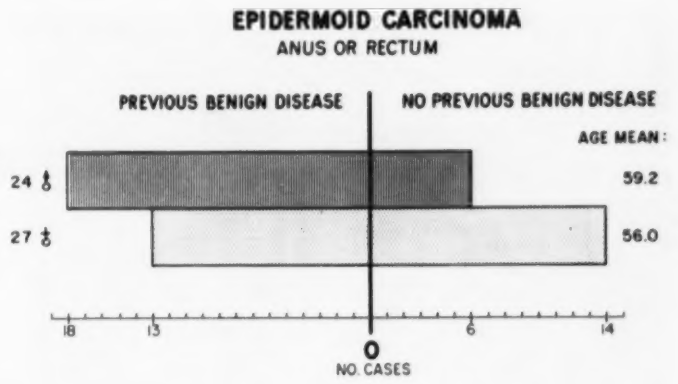

Fig. 1.—Number of men and women with and without a history of benign anorectal disease; mean age of each.

types of benign disease. It also records the number of patients who had been treated for the benign disease before the diagnosis of epidermoid carcinoma was established. In three of the nine patients hemorrhoids had been injected; in one of them, they had been twice excised. Three additional patients had experienced two or more attempts to excise the hemorrhoids. The most determined efforts had been made to treat patients with fistula. Surgical measures included drainage of perianal abscesses, unroofing, and fistulectomy. The one patient with pruritus ani had been treated with ointments, surgical excision, and external irradiation. Chronic infection, undiagnosed fissures, and probably even submucosal and subcutaneous fistulas were probably present, although undiagnosed, in some of the patients indicated as having hemorrhoids. Patients with a history of fistula perhaps had hemorrhoids as their original lesion.

The duration of the benign disease is indicated in Figure 3. Data from patients with fissures, prolapse, and pruritus have been combined, as previously indicated. Of the 31 patients with benign disease, 21 had had it for more than five years; in only 4 was the duration less than one year.

Figure 4 lists the various complaints which caused the patient to seek medical advice, resulting in hospital admission and the diagnosis of epidermoid carcinoma. Other complaints at the time of admisson included diarrhea, constipation, pruritus, and such general ones as anorexia, weakness, anemia, and malaise. A mass and drainage were more frequently the chief

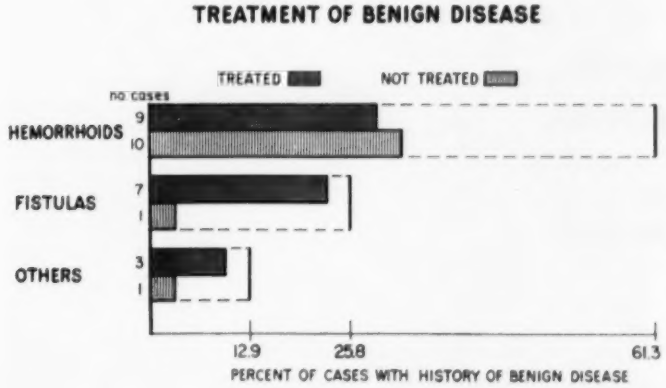

Fig. 2.—Types of benign disease (others: two patients with fissures, one with pruritus ani, and one with prolapse), number of patients previously treated and not treated for benign disease, and the per cent of all patients with history of benign anorectal disease with each type.

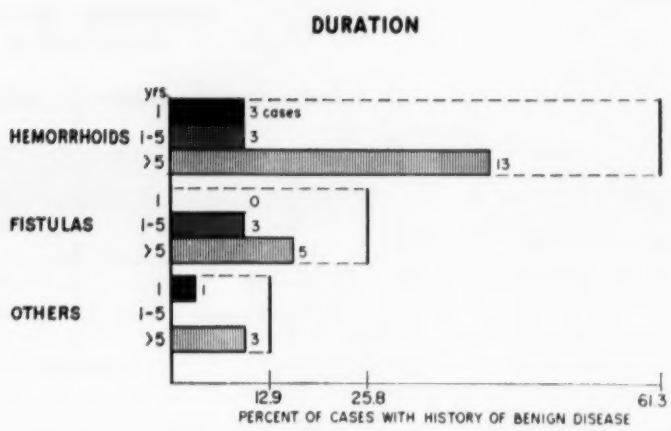

Fig. 3.—Length of time that patients had benign disease before diagnosis of epidermoid carcinoma of the anorectal canal.

complaints in the patients with a history of benign disease than in those without. The patients with chronic fistula most frequently complained of purulent drainage.

The detailed studies of the gross and histopathologic character of these neoplasms will be given in a later report. No clear-cut association of these features with a history of previous benign disease has been noted.

The location of the lesion with regard to the circumference of the anal canal or rectum did not differ in the two groups of patients, although it oftener, involved the entire circumference in those patients with a history of previous benign disease. The neoplasm was more frequently polypoid in those without a history of benign disease. Some patients without a history of benign disease had merely an area of ulceration or erosion of the anal canal or rectal mucous membrane, not grossly recognizable as a neoplasm. The lesions in both groups of patients were found occasionally presenting at the anal orifice, and sometimes within the anorectal canal at or above the pectinate line. It is sometimes difficult, and may indeed be impossible, to determine whether those within the canal originate from the anal canal and extend into the rectum or arise from the rectum (Fig. 5). Probably the neoplasm more frequently arises in the anal canal and extends either submucosally or directly into the rectum.

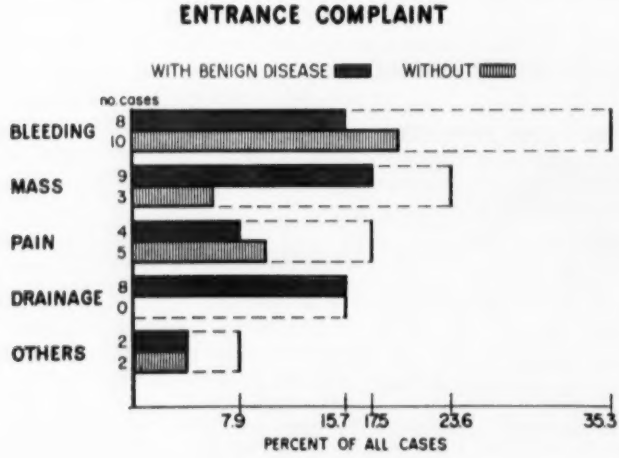

Fig. 4.—Complaint causing patients with and without benign anorectal disease to seek the medical advice when diagnosis of epidermoid carcinoma was established.

Fig. 5.—Forty-nine-year-old man. Junction of normal rectal mucous membrane (left) with moderately well-differentiated epidermoid carcinoma (right). This lesion did not present at the anal orifice. Reduced to 62% of mag. × 150.

Various degrees of histologic differentiation of the lesions were found in the two groups of patients. The failure of the histologic findings to correlate with the biologic behavior of the neoplasm is illustrated by two patients. Figure 5 is a photomicrograph of a moderately well-differentiated neoplasm in a 49-year-old man. For more than 10 years he had had hemorrhoids, which had been treated by injection. The neoplasm appeared to arise at or above the pectinate line. This patient, the only male survivor, is without evidence of recurrent neoplasm more than 14 years after abdominoperineal resection. Figure 6 is a photomicrograph of a better-differentiated lesion in a 29-year-old woman. She had had chronic anal and perineal infection, extending over a three-year period. During this period two perianal abscesses were drained, and fistulectomy was done on three occasions. This patient died of disseminated neoplasm within five months after the diagnosis was established. Well- and poorly differentiated neoplasms have been noted in both groups of patients.

In this study we have not evaluated the effectiveness of the various therapeutic measures employed in the management of these patients. They are recorded in the

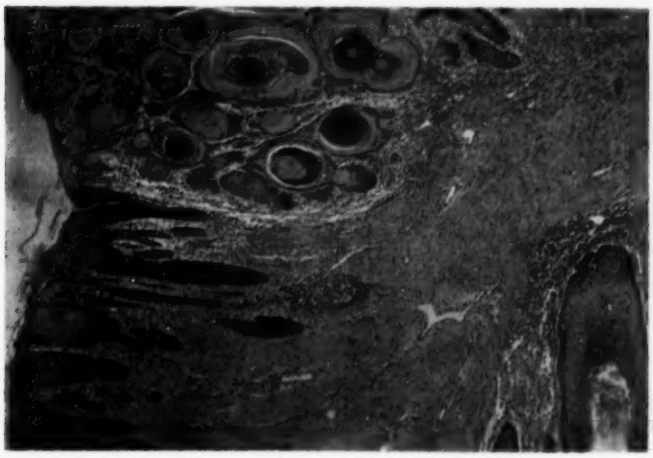

Fig. 6.—Twenty-eight-year-old woman. Junction of well-differentiated epidermoid carcinoma (above) and the normal stratified squamous-cell epithelium of the anus (below). Reduced to 62% of mag. × 150.

Therapy Employed in Patients With and Without a History of Benign Anorectal Disease

Method of Treatment	Benign Disease	No Benign Disease
Abdominoperineal resection alone	8	10
Abdominoperineal resection plus external irradiation	4	1
Abdominoperineal resection plus groin dissection	3	3
Abdominoperineal resection plus external irradiation and groin dissection	2	0
External irradiation only	4	3
Others	7	3
No treatment	3	0
Totals	31	20

accompanying Table. Among the 39 patients who had one or more operative procedures, there were 4 deaths, a mortality rate of 10.25%. One should remember that the figures include patients who had multiple formidable operations and others who had very limited surgery, such as the four who had only local excision of their carcinomas.

All patients treated by abdominoperineal resection, with or without groin dissection or irradiation or both, were regarded as having had curative therapy. Abdominoperineal resection was done only when all gross neoplasm could be resected. Palliative measures included cold therapy (three early patients), irradiation therapy, local excision, and diverting colostomy; three patients received no treatment. Just less than 45% of the men patients received curative treatment, as compared with slightly more than 74% of the women. These data are recorded in Figure 7. The difference between male and female patients receiving curative and palliative treatment is significant at the 5% level (χ^2).

Follow-up data are recorded in Figure 8. None was obtained for two men and four women; the four postoperative deaths are also omitted from this Figure. Only one man, as compared with nine women, survives. This difference between the sexes is highly significant at the 1% level (χ^2). A striking finding is that 58% of 12 women with no history of benign disease survive. The average period of survival between diagnosis and death was 1.5 years in the men and 2.6 years in the women. As has been stated, one man survives (Fig. 5). Of the nine women who survive, the most recently treated was operated upon 15 months ago; there is no evidence of recurrent or residual neoplasm. The average

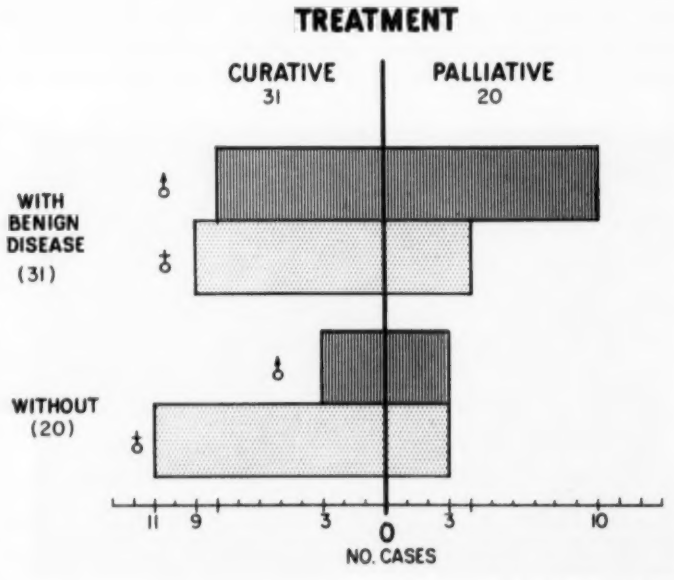

Fig. 7.—Number of male and female patients, with and without benign anorectal disease, receiving curative and palliative treatment.

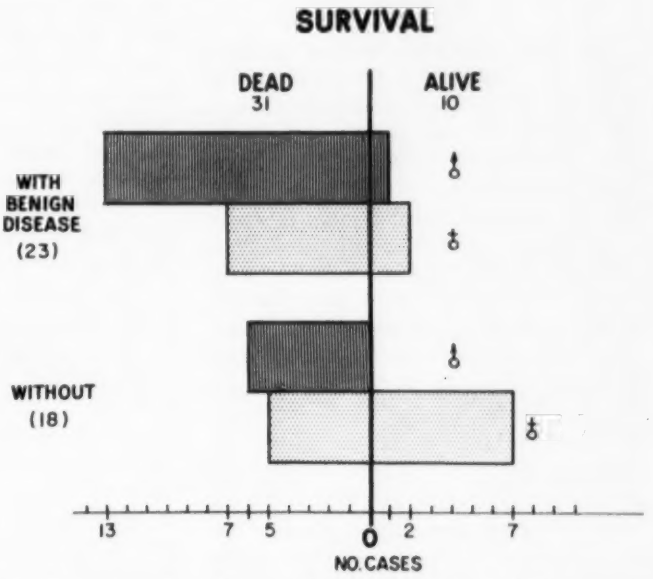

Fig. 8.—Number of male and female patients, with and without benign anorectal disease, alive and dead.

time of survival among the nine women is 4.4 years.

In Figure 9 the age, sex, and frequency of a history of benign disease in 136 patients with adenocarcinoma of the anus or rectum [5] is compared with the similar findings in 51 patients with epidermoid carcinoma.

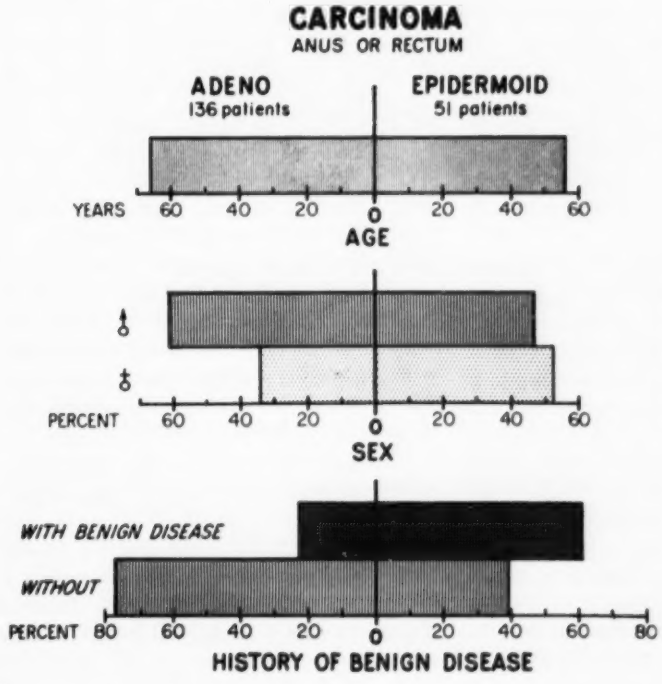

Fig. 9.—Comparison of age, sex, and frequency of a history of benign disease in patients with diagnoses of adenocarcinoma and epidermoid carcinoma of the anorectal canal.

Comment

The most important finding emerging from this study is that chronic benign anorectal disease appears to play a role in the genesis of epidermoid carcinoma in some patients. Chronic infection, many times antedating and always accompanying chronic benign anorectal disease, is a common denominator in these disorders. It is irrelevant to this discussion whether or not chronic infection is frequently a primary factor in the genesis of hemorrhoids. However, it is relevant that chronic infection invariably accompanies long-standing, symptomatic, perhaps incompletely treated hemorrhoids. In view of the known carcinogenic effects of chronic irritants, such as actinic rays, coal tar products, and radiation, we suggest that chronic infection acts as a chronic irritant and carcinogen in this instance. The reported association of this lesion to lymphogranuloma venereum [4,15] is probably on the same basis. One may plausibly postulate a similar mechanism to explain the observed higher incidence of carcinoma of the colon in patients with chronic ulcerative colitis. However, contrary to what might be expected, we are not aware of epidermoid carcinoma of the anus or rectum occurring in these patients who have had chronic diarrhea, fissure, or fistula. The explanation for this apparent contradiction may be the low incidence of both disorders.

No satisfactory explanation is apparent for the significantly different frequency of a history of benign anorectal disease in men and in women with epidermoid carcinoma. Since there is no significant difference in the frequency of hemorrhoids, fistula, and fissures between the sexes, this finding is unexpected. Apparently the lower end of the gastrointestinal tract of men is more vulnerable to the carcinogenic effects of chronic infection. It remains to be determined whether this vulnerability is related to differences of local tissue or trophic or other factors. In this connection it is of interest to remember the markedly differing frequency of epidermoid carcinoma of the lip in men and women. It seems unlikely, especially in view of the findings in populations in which pipe smoking in women is common, that the relative absence of chronic irritation alone explains this difference. Whatever the mechanism, the epithelium at the two ends of the gastrointestinal tract apparently differ in carcinoma potential in the male and in the female.

The findings suggest that there is a second type of epidermoid carcinoma of the anorectal canal, one having a different sex ratio and prognosis, and having no association with benign disease. The crux of this discussion is the criterion used in establishing the history of previous benign anorectal disease. No patients were so classified in this study unless there was an unequivocal history of symptomatic disease which had caused the patients to seek medical advice; 58% of the patients so classified had received definitive treatment for their benign disease.

The sex ratio of the 51 patients is similar to that reported by other authors. Since a history of benign disease was noted more frequently in men than in women, it follows that the incidence of the second type of epidermoid carcinoma (occurring in a patient with no history of benign disease) was substantially higher in women than in men. The significantly higher operability rate and longer survival in women than in men supports the concept of two types of lesions: (1) a lesion (commoner in men) occurring in association with chronic infection, which appears to be more lethal, with a poorer prognosis than (2) a lesion (commoner in women) occurring independent of chronic infection.

Although the data are far from conclusive on this point, they do suggest that, even though the sex ratio differs for the two types of epidermoid carcinoma, the lesions have a biologic course independent of sex (higher operability rate and longer survival in patients with no history of benign disease in men as well as women).

Other hypotheses than the one proposed—that there are two types of lesions having different etiologies and biologic courses—should be considered. In view of the evidence accumulating relative to other neoplasms, the possibility that the sex of the host affects the biologic behavior of the neoplasm must be considered. We are unaware of evidence suggesting that this lesion depends on trophic factors supplied by the host, such as estrogen for breast carcinoma. The absence of such evidence, of course, does not exclude the possibility. Anatomic differences between the sexes may lead to earlier diagnosis and, therefore, to a more favorable prognosis in women. Assuming that women are more fastidious than men, they would be less likely to go without treatment of benign anorectal disorders; likewise, they would insist on prompter and proper treatment if the initial attempt was unsuccessful. As a result, the physician would see both benign and malignant processes earlier. These factors would result in a higher operability rate of epidermoid carcinoma and a longer survival in women than in men.

Most of the preceding discussion, although of interest, must be regarded as unsupported speculation. Additional clinical studies will be necessary to determine which, if any, of these speculations may be accepted as fact. However, concrete recommendations for the clinician do emerge from this study. Benign anorectal disease should be promptly and effectively dealt with. If treatment is unsuccessful, appropriate additional measures should be promptly taken to correct the persisting difficulty. One should strongly suspect the possibility that the apparent benign lesion is, in fact, a malignant one. Histopathologic study of surgical specimens, particularly long-standing, chronically infected hemorrhoids and fistulous tracts, should be done. Biopsy of chronic fissures and fistulas is indicated. Regular follow-up examinations are essential for the patient treated for benign anorectal disease.

Summary

Evidence for an etiologic role of benign anorectal disease in the genesis of epidermoid carcinoma of the anorectal canal was found in a study of 51 patients with this diagnosis. The findings suggest the possibility of a second type of lesion, unrelated to benign disease, occurring more frequently in women, with a less lethal course than the first type, which occurs more frequently in men. Recommendations for the clinician include prompt and effective treatment of benign disorders, histopathologic examinations of specimens and biopsy of persisting areas of chronic infection, and follow-up of all patients treated for benign anorectal disease.

State University of Iowa College of Medicine.

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DISCUSSION

DR. R. KENNEDY GILCHRIST, Chicago: I think this is a most interesting subject, Dr. Buckwalter. It is one about which I have a great deal of indecision.

I well recall six cases that fall into this category —those of four women and two men. One woman is dead. She had a squamous-cell carcinoma and positive lymph nodes in the groin. A groin dissection was done, with recurrence.

One man, who is now alive, had a lesion 2 mm. in diameter at the most, not a particularly wild-looking epidermoid carcinoma, which was removed locally. Its removal was incidental to removal of a fissure and some hemorrhoids. A recurrence developed. We did not do an abdominoperineal resection, as it did not seem wise. The lesion was very small.

It is difficult for me to believe we ought to take out the rectum in such a condition, but in this patient a metastasis developed back of the hypogastric plexus along the iliac artery two or three years later.

I wonder what you do in your operation, Dr. Buckwalter. Do you do an abdominoperineal resection for all these lesions, no matter what? In how many of the eight resections was there node involvement? I am curious as to how many of the patients who had node involvement in the groin were free of disease for five years. Our own experience with those lesions is very sad. The patients have not done well.

Concerning the chronic irritation, when I first started in surgery, it seemed to me we were continually being confronted with patients who had had x-ray treatment for pruritus ani, and some of them developed carcinoma. I do not remember any of them dying, but they certainly had very extensive resections of the perianal skin, and it was not a simple problem. It seemed to me Dr. David must have had 10 or 12 such cases that I saw over a period of years. I do not believe I have seen one since 1940.

We have had one case of lymphogranuloma venereum. I had something to do with her. She developed carcinoma 15 years after defunctionalization of the bowel. Dr. David did an abdominoperineal resection, and I took out the posterior half of her vagina, and so on, and she is still free of disease, about five years later.

We have had one case of a fistula in which adenocarcinoma implants developed. The patient had a carcinoma in the colon far above this. Other than that, in my own experience I have never seen a carcinoma develop in a fistula, but I presume it must happen.

We have had a number of cases of leukoplakia. None of the patients has died, and none has had extensive resection. Some have had early change. Of course, all know the story of ulcerative colitis.

The question of two different diseases bothers me. This is a small number of cases, and I should be most interested to see what a summary of the experiences will show. It may be the author's contention will be borne out. If so, it will have a real influence on treatment of these lesions.

DR. CAMPBELL GARDNER, Montreal, Canada: I was surprised to see that the speaker included hemorrhoids as one of the precursors of carcinoma, and this diagnosis seemed to cover a fairly large number of the cases that he is presently reporting. I was not aware that hemorrhoids were a chronic infection but, rather, thought that they were varicose veins of the rectum. Does the speaker think that hemorrhoids are, or are caused by, a chronic inflammatory process?

We have not been in the habit of sending tissue removed at hemorrhoidectomy for pathologic section. It is conceivable that we may miss an incipient carcinoma in this way. I have never seen one occur in this manner; perhaps the speaker would give us the incidence of such a development.

As for fistulas or fissures, I have seen only two which have been associated with carcinoma, and in both these cases we felt that the fissure had occurred because of the friable nature of the malignant tissue; and therefore we have believed, until now at least, that the fissure occurred secondarily to the carcinoma and not vice versa. I am prepared to accept the other possibility but should like to have more definite proof.

DR. HAROLD LAUFMAN, Chicago: I arise to ask a question on a point which is unclear to me from Dr. Buckwalter's presentation.

In the group that had previous surgery, is the essayist indicating that the carcinoma arose in the healing lesion after the hemorrhoidectomy, or was carcinoma found in the specimen of the removed hemorrhoid?

If it is the thesis that chronic inflammatory change may be conducive to malignancy here, then certainly the chronically infected open wounds of the healing site following hemorrhoid-

ectomy must be implicated just as much as the chronic infection before surgery.

DR. STANLEY R. FRIESEN, Kansas City, Kan.: I recall a case which illustrates another means by which this phenomenon can occur. The patient had what was called a fissure *in ano*. I did a biopsy on the fissure, and it proved to be an adenocarcinoma. At autopsy, later, it was found that the patient had a carcinoma of the sigmoid colon, and this "fissure *in ano*" was in reality a retrograde metastasis down to the anus. There were also liver metastases.

DR. JOSEPH A. BUCKWALTER, Iowa City: I thank the discussers for their provocative comments. In answer to Dr. Zollinger's question, all long-standing hemorrhoids (all the site of chronic infection) should be examined by histopathologic section.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: Have you found any cancers?

DR. JOSEPH A. BUCKWALTER, Iowa City: We have such a case, which answers Dr. Gardner's question in part. This patient was operated upon by one of the members of our staff in the audience today. The clinical diagnosis was hemorrhoidal varices. The patient had had a previous hemorrhoidectomy. A frozen section done at operation showed epidermoid carcinoma.

In response to comments by Dr. Gilchrist, there appears to be no clear criteria upon which to base the decision of which operation to use. Of the 51 patients, 4 had local excision only. These patients had benign-looking condylomatous lesions located just distal to the anal-mucosal junction in the anal canal. Three of these four patients survive, free of disease; the other patient developed metastatic disease. I don't know the answer to the question.

We are in the process of a detailed evaluation of the effectiveness of the various forms of treatment which have been employed. This is made difficult by the fact that these patients have been seen over a period of 20-odd years, and all kinds and combinations of treatment have been used. At this time, I cannot give you any statement with regard to the place of groin dissection and other measures in the treatment of this lesion.

I think chronic infection frequently plays a role in the genesis of hemorrhoids, as is stated in most of the monographs and textbooks dealing with this subject. However, of more importance in the present context is the fact that long-standing hemorrhoids are invariably associated with chronic infection, which may or may not antedate the hemorrhoids.

Concerning Dr. Laufman's discussion, I think the question is not one of the granulating wound following hemorrhoidectomy or fissurectomy, but, rather, of the persisting infection acting as a chronic irritant. The factor of chronicity is the important thing rather than the presence of infection per se.

Diagnosis and Treatment of Aganglionosis of the Myenteric Plexus

WILLIAM L. RIKER, M.D., Chicago

One of the most important advances in pediatric surgery during the past 10 years has been the clarification of the etiology of congenital megacolon and the evolution of a satisfactory form of surgical treatment. Many newborn infants who formerly died of "volvulus of the sigmoid," or "locked bowels," have been saved, and hundreds of older children have been freed from a nightmare of laxatives, enemas, and ill health.

The logical, but unfortunate, error of blaming the dilated, hypertrophic segment of bowel for the constipation was gradually erased by the efforts of many investigators until it is generally agreed that the narrow, spastic segment of aganglionosis distal to the dilatation is the cause of the obstruction. The next logical step was to direct the surgical approach to this diseased segment, as was so ably done by Swenson in 1948.[17]

At the Children's Memorial Hospital 59 patients with congenital megacolon have been treated. It seems worth while to report the experiences in these cases and recount some of the trials and tribulations encountered in their care.

Pathology

Since the typical case of congenital megacolon has absence of the ganglion cells in the myenteric (Auerbach's) plexus, I am convinced that any surgeon who may be called upon to treat bowel obstruction in the newborn or who intends to operate upon patients with megacolon should have more than a nodding acquaintance with the appearance of the normal plexus and its cells. He may be called upon to make important decisions as to the diagnosis and extent of resection if no pathologist is available or the pathologist at hand is not well versed in this particular disease problem.

Between the inner circular and the outer longitudinal muscle layer lies the myenteric plexus, extending the entire length of the alimentary canal. One element of this plexus consists of neural spaces containing ganglion cells and neural supporting structures (Fig. 1). The ganglion cells are large with abundant cytoplasm and contain a rather large nucleus with a dense, eccentrically placed nucleolus, giving the general appearance of an "owl's eye." Interconnecting these clumps of ganglion cells are networks of nonmyelinated parasympathetic nerve fibers. Reflexes passing through this intramural networks can cause orderly peristaltic waves to pass down the intestine independent of extrinsic nerve supply.

Sympathetic or parasympathetic extrinsic nerve supply to the intestine serves to inhibit or augment these contractions. When feces are passed down the colon by this peristalsis, they fill the rectum. When the rectum is full, the rectal reflex governed by voluntary control can take place, causing contraction of the rectum and relaxing of the sphincters.

Patients with typical congenital megacolon have an absence of the ganglion cells in the myenteric plexus in various lengths of the distal colon, usually the rectosigmoid. The neural space may still be visible. Indeed, the nonmyelinated parasympathetic

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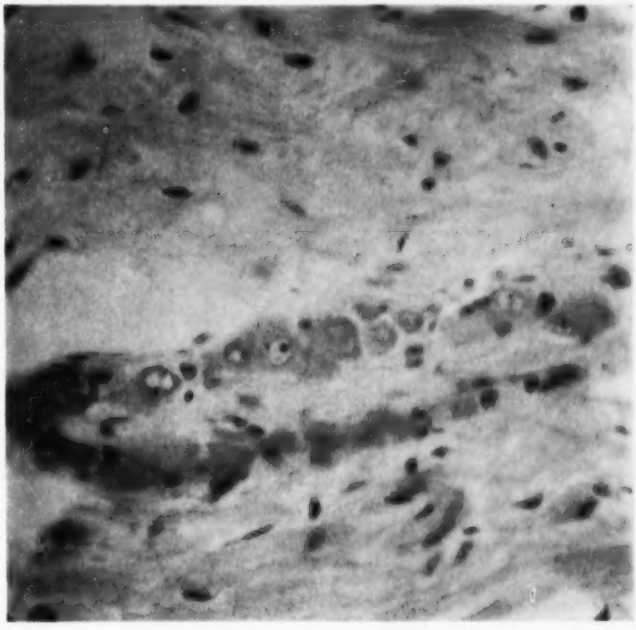


Fig. 1.—Neural space in the myenteric (Auerbach's) plexus in the colon can be seen lying between the inner circular and the outer longitudinal muscle layer. Typical ganglion cells are plentiful and contain large nuclei with eccentrically placed nucleoli, resembling owl's eyes.

nerve bundles are usually more prominent than normal (Fig. 2).

Various theories have been advanced to explain this developmental anomaly. The one suggested by Bodian [4] seems most plausible. The ganglion cells are presumably formed intramurally in a cephalad to caudad progression. If their formation at some stage is arrested, there will be agenesis from that point distally to the end of the bowel. Figure 3 shows the extent of the aganglionosis in 51 of the cases in which complete pathological examination of the surgical specimens or autopsy material was performed. Sporadic reports of zonal aganglionosis with normal nerve cells above

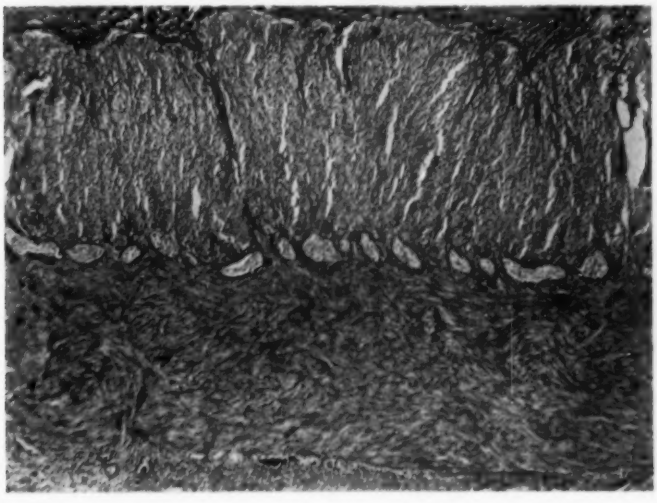
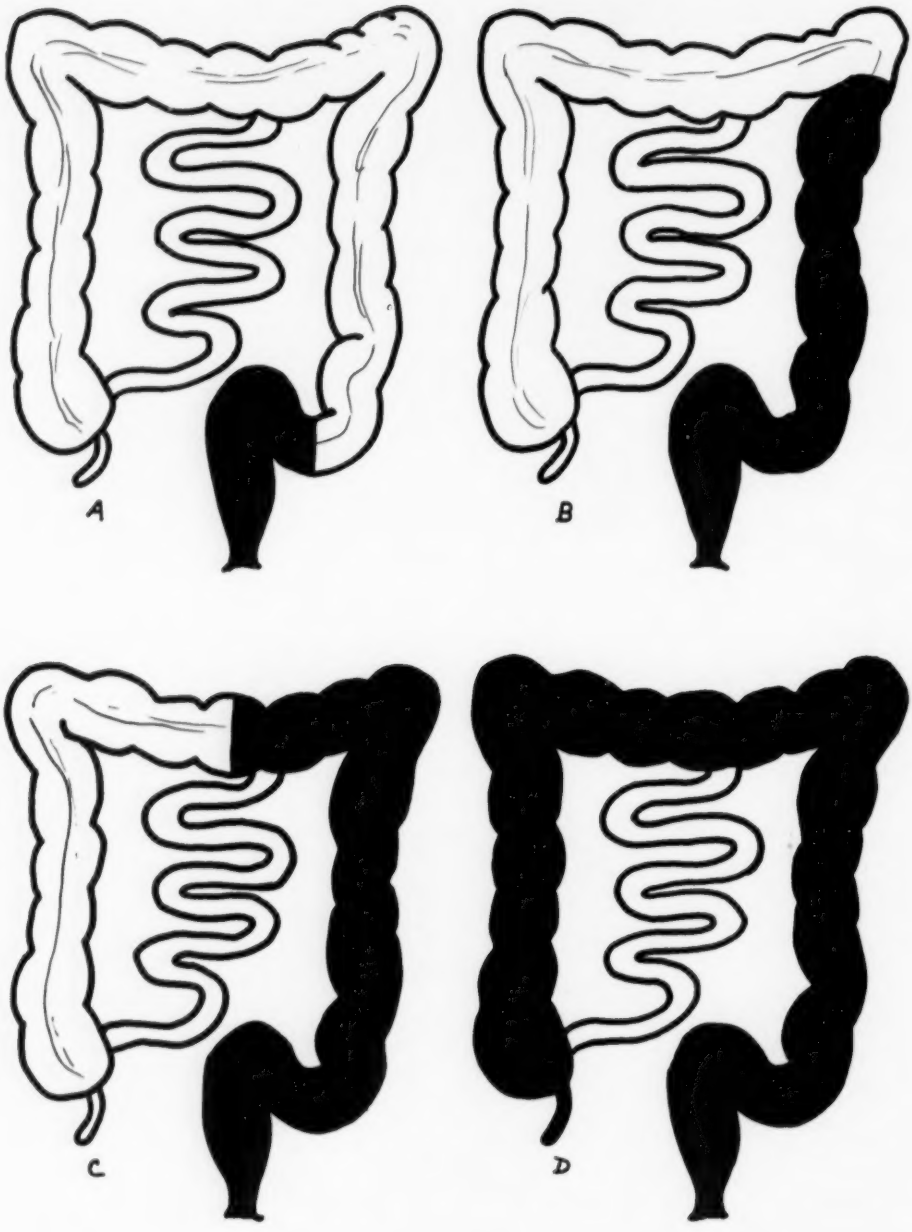


Fig. 2.—In a case of aganglionosis of the myenteric plexus there is often an increase in the bundles of nonmyelinated nerve fibers between the muscle layers, but collections of ganglion cells are absent.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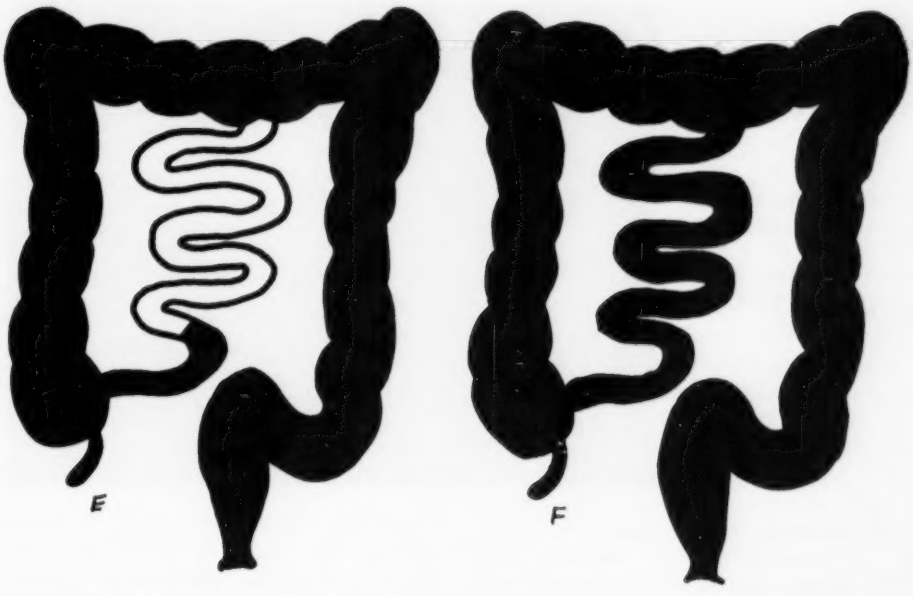


Fig. 3.—Diagrams of the extent of aganglionosis in 51 cases in which adequate pathological examination was available.
A, aganglionosis of rectosigmoid (29 cases); *B*, aganglionosis to splenic flexure (6 cases); *C*, aganglionosis to transverse colon (10 cases); *D*, aganglionosis of entire colon (3 cases); *E*, aganglionosis of entire colon and terminal ileum (1 case); *F*, aganglionosis from anus to duodenum (2 cases).

and below have appeared.[10,11] All of our cases exhibited lack of ganglion cells from the point of aganglionosis all the way down to the anus or the lowest portion of the resected specimen, usually only a few centimeters from the anal margin.

The painstaking examination of the specimens by our pathologist, Dr. Joseph Boggs, has involved removing a narrow strip of bowel wall extending the entire length of the specimen. It is cut into convenient lengths to fit microscopic slides, which are then numbered from the caudal to the cephalic end. This allows accurate millimeter-by-millimeter examination for the extent and character of the aganglionosis. The extent of the bowel resection, as noted by the uppermost level of transection reported by the surgeon, was correlated with the length of the segment removed and the exact point of microscopic transition to normal ganglion cells in order to arrive at the approximate level of aganglionosis in the colon.

Most reports cite the figures of 90% short-segment aganglionosis, involving only the rectosigmoid, and 10% long-segment aganglionosis, involving more than the rectosigmoid. In this series it will be noted that over 40% of our cases involved bowel above the rectosigmoid, including two patients in whom the pathology extended from the anus to the duodenum.

Of 22 patients with severe obstruction in the neonatal period having adequate pathological examination, the aganglionosis was of long-segment type in 12, extending to the splenic flexure in 1 case, to the transverse colon in 6 cases, throughout the entire colon in 2 cases, the entire colon and the terminal ileum in 1 case, and up to the duodenum in 2 cases. This preponderance of long-segment involvement has affected our plan of placement of colostomy.

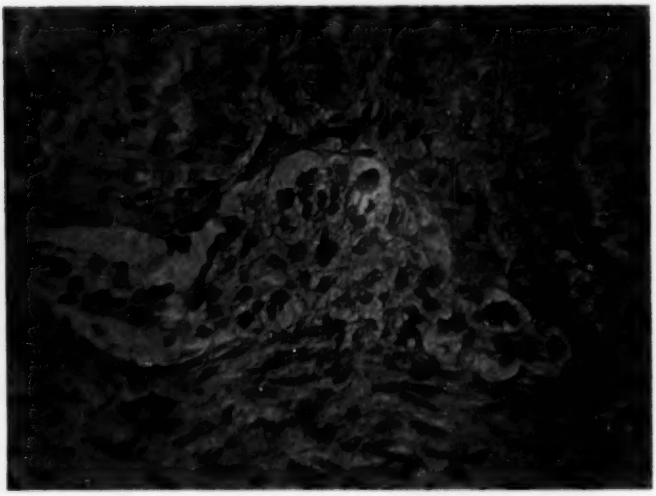


Fig. 4.—Dysgenesis of myenteric plexus. The neural spaces are present but contain no normal ganglion cells. What cells are present are distorted and few.

Aganglionosis of the myenteric plexus is often presented as a cut-and-dried entity, with complete absence of ganglion cells to a certain point in the distal colon, then a short segment of transition with increasing number of cells, just above which the ganglion cells are present in normal number. Several cases have not shown this absolute "all-or-none" appearance. Instead, an occasional ganglion cell may be scattered throughout various sections of the diseased bowel (Fig. 4). These cells are usually definitely abnormal in appearance and apparently malfunctioning. In several of these instances there has also been an absence of the prominence of intermuscular nerve bundles usually associated with a typical agenesis.

Two patients with their disease involving the intestine from the anus to the duodenum exhibited not only aganglionosis throughout the entire segment but also decreased parasympathetic nerve fibers (Fig. 5). It has been suggested that failure of the extrinsic innervation to enter into the intramural space may result in the failure of development of ganglion cells in the myenteric

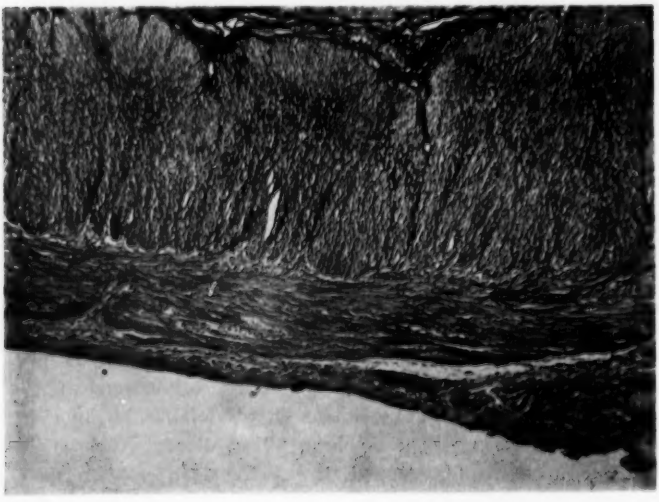


Fig. 5.—Unusual type of aganglionosis with absence of all neural elements, including nerve bundles, as well as ganglion cells and neural spaces.

plexus or that the lack of innervation may cause their degeneration.[5]

The physiological effect of the typical aganglionosis has been studied with balloon-and-pressure tracing by Swenson [18] and Hiatt,[7] demonstrating orderly propulsive peristaltic contractions of the proximal bowel. This is carried on by the reflexes in the normal intramural networks of the myenteric plexus. The ganglion cells are responsible for coordinating these rhythmical contractions into orderly peristalsis. When the nerve impulses reach the aganglionic segment, they pass into the abundant network of nerves already described and without the supervision of ganglion cells result in uncoordinated mass contraction of the segment. This physiological block to passage of feces results in dilatation of the proximal bowel and hypertrophy of the muscular wall in an attempt to overcome the obstruction. Another factor that increases the constipation is the failure of the rectal reflex. Since feces have difficulty in reaching the rectum, the reflex cannot be initiated. Even when feces are finally forced into the rectum, the faulty intrinsic innervation makes the reflex contraction of the rectum and relaxation of the anal sphincters ineffective.

The persistent attempts of the distal bowel to push feces past the aganglionic segment may dilate the uppermost section of this diseased portion of bowel, causing its musculature to hypertrophy. It is suggested that the disordinated mass contraction of this aganglionic section with its increase in muscular power results in an increasing obstruction to passage of feces.[7] This may explain the apparent increase in constipation in certain patients as they get older.

Continued distention of a short aganglionic segment in the rectum may cause the dilatation to extend down to the anus. Thus, megarectum may not always indicate the idiopathic or acquired type of megacolon but may actually represent a resectable case of aganglionosis.

Diagnosis

Symptomatically and therapeutically, the cases of aganglionosis may be divided into two groups—the neonatal cases with a high degree of obstruction, requiring immediate operative intervention, and the cases of a less severe form, which allows the patients to live for several months or years in a state of chronic constipation.

Neonatal Cases.—These cases, with complete or partial intestinal obstruction, must be evaluated carefully, since agenesis of the myenteric plexus may be the cause. Vomiting of bile, abdominal distention, and failure to pass stools are symptoms of several serious conditions in the newborn. Stenosis and atresia of the bowel, meconium ileus, meconium peritonitis, imperforate anus, malrotation of the intestine, and duplication of the intestine are some of the possibilities to be considered.

The passage of even small amounts of meconium serves to rule out several of the above conditions. Frequently, an enema, or even a rectal examination, will produce a large evacuation of stool and gas in the newborn child with aganglionosis. This must not lull one into complacence, since many infants with congenital megacolon were sent home, only to return in poor condition with recurrent obstruction requiring immediate surgery.

Upright and supine roentgenograms of the abdomen show signs of obstruction with gas-filled, distended loops of bowel and air-fluid levels (Fig. 6). If a portion of the distended bowel can be identified as colon and the rectum can be seen to be empty of gas and feces, aganglionosis is the most likely cause of the obstruction. If the patient's condition is satisfactory, a barium enema study may be done. In only five infants in the neonatal period have we demonstrated typical roentgenographic findings of a narrow rectosigmoid colon and an abrupt transition of dilated proximal colon (Fig. 7). Berman [2] reports positive colon fluoroscopic findings in 15 of 19 patients less than 5 weeks of age, as evidenced by discovery

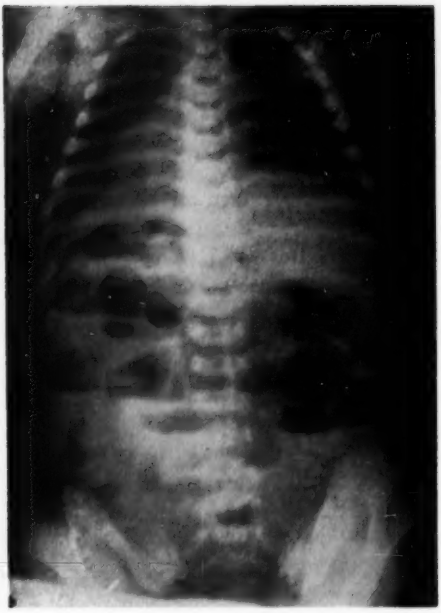


Fig. 6.—Roentgenogram of a newborn infant's abdomen in the upright position showing distended loops of bowel and air-fluid levels, some of which may be in the colon. The rectum is empty.

of a transition zone or prolonged retention of barium in the colon.

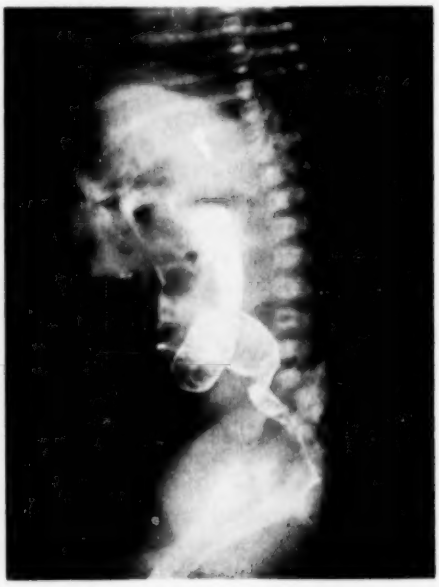
Of 24 patients treated during the neonatal period, 12 required surgery within the first week of life. The others temporarily recovered from their acute obstruction and went home but were plagued by constipation or diarrhea, intermittent vomiting, dehydration, and malnutrition, until they returned in a few weeks for surgery.

Older Group.—Thirty-five patients in this series survived without therapy until later infancy or childhood and were first seen for diagnosis and therapy at from 2 months to 13 years of age.

These patients presented various histories. Usually there had been constipation since birth. Often there was either diarrhea due to irritation of the bowel wall by fecal stasis or a paradoxical diarrhea around a fecal impaction. One patient allegedly had had no constipation for the first 3 years of life. He then had two attacks of obstruction, necessitating resection, at 4 years of age. He had a typical aganglionosis of the rectosigmoid. This apparent failure of the general rule (no constipation from birth—no agenesis of the myenteric plexus) may have resulted from the older brother's severe symptoms of the same disease overshadowing the younger patient's rather mild difficulties. Many of the patients had a history of one or more attacks of acute obstruction with vomiting, dehydration, and electrolyte imbalance, requiring hospitalization.

Abdominal distention with bowel patterning, palpable fecal mass in the sigmoid with an empty rectum, foul stools, anemia, and generally poor development were all prominent symptoms. The general debility and lack of resistance to respiratory infections, so often present, should prompt one to advocate surgery as soon as the diagnosis has been established. Two of our patients were hospitalized awaiting surgery. Just the day before his operation was scheduled, each child developed a respiratory infection. In

Fig. 7.—Lateral, postevacuation roentgenogram after barium enema in a newborn infant. There is a narrow rectum with abrupt transition in caliber in the sigmoid to the dilated descending colon.



spite of vigorous therapy, both died of pneumonia and bacteremia.

The classical history and findings associated with megacolon are not enough, since partial mechanical obstruction and idiopathic or acquired megacolon may give the same picture. Fluoroscopic examination of the rectosigmoid with a barium enema in most instances will establish the diagnosis. We have used essentially the same method as that described by Neuhauser.[19] The child is placed in the left lateral decubitus position on the fluoroscopy table. A plastic enema tip with a bulb at the end is inserted into the rectum just far enough that the enlarged end is immediately above the sphincters. The barium material is introduced slowly and observed in various positions under fluoroscopy. Spot films record the findings of a relatively narrow "spastic segment" in the rectum and rectosigmoid juncture, with sudden transition to dilated colon (Fig. 8). To introduce barium farther up into the colon is unnecessary and dangerous, since impaction or water intoxication may result. Post-evacuation films are routinely taken and may show the "spastic segment" better than the films taken during the filling process, owing to overlapping of loops of bowel or overdistention of the narrow segment.

Fig. 8.—Lateral roentgenogram during barium enema in a child with aganglionosis of the rectosigmoid. The "spastic" rectum can be seen, with abrupt widening to a greatly dilated colon above.

We have had one "false-negative" barium enema examination in a 3-year-old child. A typical rectosigmoid aganglionosis was found at operation. There has been no false-positive examination to date, although some have been reported.[1] There seems to be no exact correlation between the level of transition in caliber as seen by roentgenographic examination and the actual microscopic level of aganglionosis except when the entire colon is involved. Reports of a spastic rectosigmoid with abrupt transition in the upper sigmoid were given in several cases in which the aganglionosis extended to the splenic flexure or transverse colon.

Rectal biopsy, as advocated by Swenson[21] and Bill[1] and their associates, has not been used in this series. It may be indicated in a patient with an atypical history, such as that of diarrhea or a late development of constipation. Atypical roentgenographic findings may also be an indication for rectal biopsy, as in cases of dilatation of the large bowel to the anus, or of aganglionosis involving the entire colon, or of colostomy in which the diagnostic differential in caliber is lost.

The incidence of boys to girls was 42:17. This relatively high incidence of the disease in girls is different from that in most reported series, in which the male-to-female ratio often approached 10:1.

It was also interesting that association of other congenital anomalies with congenital megacolon was relatively infrequent. Only two patients had major defects. One was a girl with an imperforate anus, which had been repaired at birth. Colon biopsy during exploratory laparotomy at 3 years of age showed very rare and distorted ganglion cells, and the history and roentgenographic findings were suggestive. No surgical treatment is contemplated, since she depends largely on constipation for

fecal "continence." The second child was a female infant with cerebral dysgenesis and endocardial fibroelastosis, in addition to her aganglionosis.

Six children in this group had a familial history of megacolon. Two were brothers who were operated upon and proved to have aganglionosis of the rectosigmoid. The newborn brother and sister with aganglionosis from anus to duodenum have been mentioned above. An 11-year-old girl with aganglionosis to the middle of the transverse colon had a father who had had constipation from birth, requiring five operations, including three colon resections, before he was relieved of symptoms. An additional infant with aganglionosis had had a sibling who died at birth of "twisted bowels."

Treatment

The high mortality rate with medical management, especially in the younger age groups, would suggest that such a conservative program be used only in mild cases which respond well to a regimen of drugs, dietary management, and occasional enemas.

When the care of the bowel management becomes a burden, both physically and emotionally to the patient and to the parents, operation should be considered. Repeated impactions or episodes of acute obstruction should prompt surgery. Malnutrition and continued ill health also indicate that medical management has failed and that surgery must be done. The occurrence of two fatal respiratory infections in hospitalized patients awaiting operation, as mentioned above, must not be an isolated experience. Certainly, many children must die of such infections while on medical regimens.

Preoperative Care.—Preparation of the bowel and that of the patient are of equal importance. The patient must be got into good enough condition to undergo a rather serious operation and be able to heal his wounds well postoperatively. This preparation includes an adequate diet, a high vitamin intake, transfusions as necessary, and antibiotics to prevent infections. Preparation of the bowel entails complete emptying of the colon and as much sterilization of its contents as possible.

To empty the bowel, large and repeated enemas are necessary. The rectal tube must be inserted far enough to clear the spastic segment and enter the area of fecal impaction that most of these children have. Enemas of as much as several quarts of fluid may be necessary in the older patients. Isotonic saline solution is routinely employed to avoid the water intoxication syndrome reported by others.[7,9,14] It has been suggested that in cases with low cardiac or renal reserve the irrigation fluid should consist of an isotonic solution of gelatin or agar. We have never had occasion to use either of these solutions.

Another complication of the use of enemas is perforation of the colon. Lee reported two such cases, and we have seen perforation twice. One 3-week-old infant entered the hospital with peritonitis and pericecal abscess. This was most likely due to perforation, since after peritoneal drainage a fecal fistula developed. It is possible that the frequent enemas given for constipation since birth might have caused the perforation. Subsequently, agenesis of the entire colon was proved. Another infant, 7 days old, had been given repeated enemas since birth. When he entered the Children's Memorial Hospital, he seemed to be in fairly good condition, but at fluoroscopy not only did the barium enema show a typical picture of aganglionosis but there was an immediate outpouring into the peritoneal cavity (Fig. 9). Colostomy and closure of the perforation and a subsequent resection of half the colon gave excellent results.

Although many antibiotics are satisfactory for bowel sterilization, neomycin has been used routinely for several years and has been quite effective.

Intravenous pyelograms are performed before operation, but no case of megaloureter has been observed.

Fig. 9.—Roentgenogram of a newborn child after barium enema. A typical transition zone diagnostic of aganglionosis was seen, but, to our surprise, the barium also ran out into the peritoneal cavity (see text).

Operation.—For surgical treatment these patients may be divided into two categories: the newborn infant with obstruction and the constipated older infant or child.

Newborn Infant: After many struggles with this disease in the newborn, our current program is to do a colostomy on any infant with obstruction at birth due to aganglionosis. Even if the obstruction is temporarily overcome by enemas, the patient usually is brought back to the hospital with reobstruction, and often in critical condition.

Resection and primary anastomosis in the newborn would be desirable, and Lee [11] reported success in a 6-day-old child. The infants we see are usually in poor condition due to delay in diagnosis because of the incomplete nature of the obstruction. The passage of even a small amount of meconium encourages the physician to make prolonged attempts to treat the condition nonsurgically. One patient in this series was treated by resection and primary intraperitoneal anastomosis at the age of 2 days. Leakage of the anastomosis resulted in peritonitis and death. Since colostomy and secondary anastomosis have resulted in no deaths over the past five years in this age group, we have been reluctant to try primary anastomosis again.

The site of colostomy is still debatable. Although many surgeons advocate a sigmoid colostomy, and it was suggested in a previous communication from Children's Memorial Hospital,[13] this site has never been used by us. The incidence of long-segment aganglionosis of more than 50% in our series of newborn infants has ruled against the routine use of sigmoidostomy. Of 22 patients studied adequately as to the level of aganglionosis, only 10 had short-segment aganglionosis involving only the rectosigmoid. Of the other infants, seven needed a transverse colostomy, and three, an ileostomy and two patients with aganglionosis of most of the intestine were untreatable. Therefore, in order to be sure of treating most of our cases satisfactorily, a transverse colostomy seemed necessary.

Prior to the colostomy, a left lower-paramedian laparotomy incision is made, and exploration for any mechanical obstruction is done. A biopsy specimen of the rectosigmoid is taken to give documentary evidence of the presence of the disease. Usually, frozen-section studies are done to reassure the surgeon and to prove to the inherently disbelieving residents that the colostomy was necessary in the absence of any apparent cause of intestinal obstruction. The biopsy done at the time of colostomy eliminates the possibility of resecting normal colon at a later date, as has been reported.[1]

The fecal stream should be diverted completely from the distal colon by a double-barreled colostomy (Fig. 10). A small transrectus incision is made in the left upper quadrant, and a loop of mid transverse colon is gently brought out onto the abdominal wall. This loop is kept in position by a glass rod and rubber tube loop, not by suturing the seromuscular layer of the bowel to the

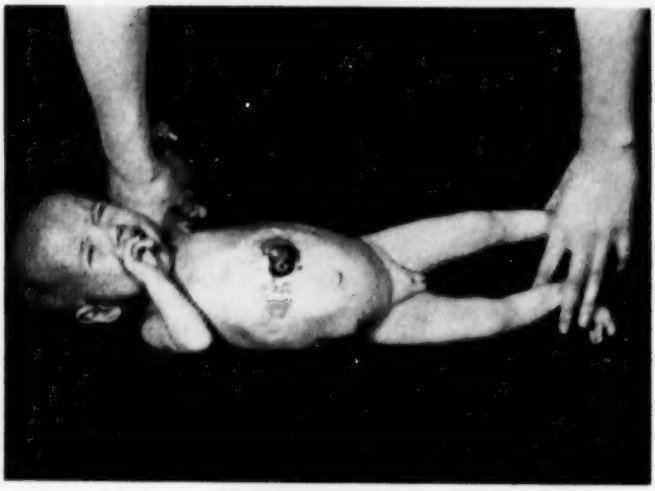


Fig. 10.—Location of the transverse colostomy performed in the newborn with severe obstruction due to aganglionosis is demonstrated. A previous ileostomy, which led to dehydration and electrolyte imbalance, has been closed.

wound edges. Such stitches taken in the infant's thin, distended bowel wall will usually result in leakage at the site of their placement. The wound is snugged about the loop of bowel, but not tight enough to interfere with its blood supply or the patency of its lumen. A piece of iodoform gauze placed between the skin edges and the bowel wall may hasten adherence. In two cases evisceration of the loop of colon occurred, but replacement was accomplished without undue difficulty.

On the day following the operation a biopsy specimen of the anterior wall of the loop of colon is taken and the colostomy is opened by cautery. This biopsy usually proves the presence of normal ganglion cells. Their absence at this site would suggest that an ileostomy is necessary. Earlier difficulties with leakage, peritonitis, and adhesions have been overcome. With adequate attention to fluid and electrolyte therapy immediately postoperatively and to diet later, the colostomies have not been a great problem in general.

About six months after colostomy the child is usually thriving and ready for the final procedure. The bowel is prepared by means of oral neomycin and enemas in the proximal colostomy loop. The distal colon is irrigated with a solution containing neomycin.

The left paramedian incision is reopened, and clamps are placed on the afferent and efferent colostomy loops from inside the abdomen. The bowel at the colostomy site is excised. The proximal end of the colon is closed with an over-and-over silk suture, leaving the ends long.

The mesentery of the left colon and its vessels are divided, and dissection is carried down along the rectum until the insertion of the levators is reached. Two clamps are placed across the lower sigmoid, and the left colon is removed. The sigmoid stump is closed with a continuous silk suture. The two ends of this suture are each tied to the corresponding ends of the proximal-colon suture.

The anus is then dilated and the sigmoid grasped from inside with a sponge forceps and pulled down outside the anus, bringing with it the proximal colon. The mobility of the transverse colon permits it to be brought down easily, though the midcolic artery often must be divided. No impairment of blood supply has been noted.

The anastomosis is performed 1 or 2 cm. outside the anus, using interrupted 0000 silk sutures in the seromuscular layer and interrupted 00000 chromic absorbable surgical sutures in the mucosa.

Gastric suction is maintained for a day or two, until peristalsis is heard. The ure-

thral catheter put in at operation is usually removed the second day. No urinary retention has been noted in these infants. Broad-spectrum antibiotics are continued for a week postoperatively, and the patient usually leaves the hospital in 10 days or 2 weeks.

Older Group: The operation performed upon the older infants and children has usually been a resection and pull-through anastomosis without prior colostomy. It was often necessary to resect the dilated colon proximal to the aganglionic segment before the pull-through because of the mechanical difficulties with its size. Closure of the free ends by suture and tying them together will allow them to be pulled down simultaneously, as described above.

Biopsy and frozen-section examination of the spastic segment and proximal bowel are always done. Even though the transition in size and appearance is striking at operation (Fig. 11), the area of absence of ganglion cells may extend well into the dilated portion, and biopsy specimens must be obtained farther up the colon, until the cells are normal in both appearance and number. The biopsy specimen of seromuscular layers, leaving the mucosa intact, as described by Lee,[11] has been found satisfactory and prevents peritoneal contamination.

For several years the pull-through anastomosis was used successfully. Then, in 1952, the operation suggested by State[15,16] was adopted because of fear of interfering with the nerves of the urogenital region. A series of complications in 16 patients who had this low intraperitoneal anastomosis consisted of three leakages at the anastomosis requiring colostomy, and one case of leakage and death. The pull-through anastomosis was reverted to and is our present preference. If dissection of the rectum is kept close to the fascia propria, interference with the nerve supply to the urogenital organs seems unlikely.

In general, the postoperative care was similar to that of the infants described above. The catheter was kept in the bladder longer because atony of the bladder seemed more of a problem here than in the younger group.

Results.—Of the group of 24 newborn infants with aganglionosis, 12 patients had definitive surgery completed. One of the infants who had a primary resection developed leakage at the anastomosis and died, as mentioned above. The survivors have all done quite well. One mild stricture at anastomosis was easily dilated. One patient has had a colostomy and is awaiting colon resection.

Fig. 11.—Appearance of the colon at operation demonstrating the narrow rectosigmoid and abrupt transition to the dilated colon with hypertrophic musculature. This gross examination must not be depended upon to indicate the extent of aganglionosis and the amount of bowel to be resected. Biopsy and frozen-section study must be relied upon to prove the uppermost extent of the disease.

The other 11 infants died of various causes. One patient was 6 days old when brought to the hospital in a moribund condition, distended, cyanotic, and in shock. Gastric suction, oxygen therapy, and a blood transfusion were started, without improvement in his condition. He was scheduled for colostomy under local anesthesia but died before it could be done. Autopsy showed gangrene of the distended wall of the colon and aganglionosis of the rectosigmoid.

Three of the infants that died had exploratory laparotomies only. One patient having aganglionosis to the duodenum had two explorations, with biopsies demonstrating agenesis in the colon. In another patient, operated upon previously for "volvulus of the sigmoid," the abdomen was reopened and an extensive peritonitis found. The third patient had an exploration in 1948, before we were aware of this disease entity, and died one month later.

Four patients had had a transverse colostomy before they died. Three of these died of adhesions or peritonitis. Such complications have not occurred during the past five years. The fourth child had a colostomy which functioned poorly. Autopsy at 2 months of age showed aganglionosis of the entire colon.

The last three patients had a very-long-segment type of aganglionosis. One child with aganglionosis to the duodenum had an ileostomy which failed to function. The other two fatalities were in children with aganglionosis of the entire colon, one extending into the terminal part of the ileum. In one instance the condition was not suspected because peritonitis and abscess formation were found primarily. In the other infant a biopsy of the ileum showed aganglionosis. No ileostomy was done; the biopsy site broke down, and the child died of peritonitis.

The three patients with aganglionosis of the entire colon were ones that might have been saved by ileostomy followed by secondary ileoproctostomy.[20]

Complications in the older age group were related primarily to troubles at the site of anastomosis. Twenty-eight colon resections and anastomoses were performed in children from 3 months to 13 years of age. Thirteen patients had low intraperitoneal anastomoses, of which three leaked, necessitating temporary colostomy. Eventually these patients attained excellent bowel function.

Fifteen patients had the pull-through type of anastomosis. Two patients developed leakage at the anastomosis and died. A colostomy in one case and an ileostomy in the other failed to save them.

This high incidence of 6 anastomotic leaks in a total of 40 infants and children having resections is rather alarming. The placement of drains in the pelvis or presacral space did not have any effect on this complication and has been abandoned. As suggested by Lee,[11] the abscesses that form are secondary to leaks at the anastomotic line, not vice versa. Poor blood supply of the proximal bowel was blamed in some instances, but it is difficult to prove that it was the cause.

Lee's explanation that the ends of the silk stitches in the seromuscular layer may protrude into the bowel lumen might explain leakage in the patients with the pull-through type of anastomosis but would not account for four leakages in the patients undergoing low intraperitoneal anastomosis.

Four patients in this older age group died, having had no definitive operation. The two patients who died of pneumonia just prior to surgery were already mentioned. Another child, a 3½-year-old girl, came to the hospital in critical condition with complete obstruction, unrelieved by rectal irrigation. Cecostomy was ineffective, and the patient died. Aganglionosis of the entire colon was found at autopsy. The fourth child was a 5-month-old infant seen in 1947. In spite of an ileostomy, the patient died, and aganglionosis of the rectosigmoid was found at autopsy.

The final 3 patients of the total of 59 have congenital megacolon, proved by history, roentgenography, and, in one case, biopsy. Two patients are awaiting surgery, and one, with repair of an imperforate anus, as mentioned above, will not be operated upon.

Other postoperative complications than death and leakage of the anastomosis were atony of the bladder, which was troublesome in two patients, and an easily dilated stricture at the anastomosis, in one patient. One patient has had constipation postoperatively, requiring several hospitalizations for fecal impactions. Review of the pathological findings shows that the ganglion cells were sparse and atypical in the descending colon, which was used for anastomosis.

In two patients, operated upon in 1950, the dilated segment was so hyperemic and thickened that the surgeon was lured into removing only this section of colon. Recurrence of symptoms and roentgen findings within six months in both instances necessitated reoperation and removal of the aganglionic segment with complete relief of the condition.

Summary

The pathology and physiology of aganglionosis of the myenteric plexus is a problem with which all surgeons should be acquainted.

Aganglionosis in the newborn presents signs and symptoms of acute obstruction, requiring prompt surgical treatment.

In this age group an exploratory laparotomy, biopsy of the rectosigmoid colon, and transverse colostomy are done at once, followed in six months by resection of the left half of the colon and a pull-through anastomosis.

In the older age groups a primary resection and pull-through anastomosis are done.

Experiences with 59 patients with aganglionosis of the bowel are reviewed and the results of treatment discussed.

104 S. Michigan Ave. (3).

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Staphylococcal Enterocolitis

DERWARD LEPLEY Jr., M.D., Wood, Wis., and MILES B. SMITH, M.D., Milwaukee

Staphylococcal enterocolitis has recently become a serious problem on the surgical service of this hospital. This paper presents 16 bacteriologically proved cases which have occurred since 1953, in all of which the patient survived. Many of these patients were critically ill and survived only because of early diagnosis, early adequate treatment, and close physician supervision. Emphasis is placed on treatment of dehydration, hypovolemia, and shock. We believe that cross infection plays an important role in the pathogenesis. Prophylaxis should be directed toward control of cross infection and judicious use of antibiotics. The clinical picture and treatment are discussed, and three cases are presented in detail.

History

The relationship of this disease to the pseudomembranous enterocolitis which occurred prior to the antibiotic era has not been definitely established. The latter disease was first described by Finney in 1893.[10] In 1939 Penner and Bernheim[27] presented a study of 40 autopsy cases and concluded that shock was the primary etiologic agent. Kleckner, Bargen, and Baggenstoss[20] reviewed the autopsy cases at the Mayo Clinic for an 11-year period and found that all the patients had presented profound shock.

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From the Surgical Service, Veterans' Administration Hospital, Wood, Wis., and the Department of Surgery, Marquette University School of Medicine, Milwaukee.

Resident in Thoracic Surgery, Veterans' Administration Hospital; Clinical Instructor in Surgery (Dr. Lepley). Chief, Surgical Service, Veterans' Administration Hospital; Assistant Clinical Professor of Surgery (Dr. Smith).

The relationship of antibiotics has become extremely controversial the past 10 years, but Pettet et al. in 1954[26] reviewed Mayo Clinic records from 1925 to 1952 and found an almost equal incidence in the preantibiotic and antibiotic eras. They noted that 77 of 94 patients had operations upon the gastrointestinal tract. From this review they also decided that shock was secondary and due to electrolyte imbalance.

Speare[35] in 1954 presented an excellent study of eight cases of staphylococcal pseudomembranous enterocolitis. In five of the cases hemolytic Staphylococcus aureus (Micrococcus pyogenes var. aureus) was isolated from the stool culture. He considered the disease a complication of antibiotic therapy. Since 1953 numerous authors[11,18,32,38] have contributed to the literature and identified the disease as a staphylococcal infection, but some[30] still feel that the Staphylococcus is responsible for only a portion of the cases of enterocolitis reported.

Several authors[16,35,36] have suggested that the routine use of culture media for stool culture which suppress growth of other organisms would result in isolating the Staphlococcus more frequently.

A review of the literature reveals that very few cases were reported prior to 1952 in which Staphylococcus was found and incriminated as a causative agent. Case reports from 18 articles since 1952, however, totaling 66 patients, reveal that 48, or 72.7%, had Staphylococcus isolated from the stool culture. Forty-six per cent of these patients survived.

Clinical Picture

The clinical picture of staphylococcal enterocolitis has been described as a

"choleriformic syndrome." The patient may be doing well in the immediate postoperative period, when suddenly, with no apparent cause, he becomes anorexic and complains of abdominal distention and pain. The pulse rises to 130-150 per minute; fever, with the temperature up to 105-106 F, occurs, and the patient may become lethargic or semicomatose. He may be dyspneic and complain of sore throat or sore tongue. These symptoms may be preceded or followed by a severe watery diarrhea, which progresses in intensity during the following 48 hours. If unchecked, electrolyte and fluid losses are massive and oliguria ensues. Mild hypotension will be present early, but, if untreated, severe circulatory collapse occurs and, if prolonged, may be irreversible.

The diarrhea is characterized by "rice-water stools." The stools have no formed elements and at first appear to be like plasma and have a fetid odor instead of a fecal one. Later the stools may become a black or green liquid.

In the surgical patient this disease usually occurs in the first five days of the postoperative period. Before diarrhea occurs, the physician confronted with the above-described picture is prone to incriminate a leaking intestinal anastomosis or peritonitis. Atelectasis may also accompany the disease, and at this stage of postoperative recovery it is suspected as the explanation for the signs and symptoms, delaying proper therapy.

Pathogenesis

The disease appears to be a superinfection occurring with increased incidence in the past few years, concomitant with widespread antibiotic therapy. The etiologic agent is an antibiotic-resistant, coagulase-positive hemolytic S. aureus. In the usual case the patient has been operated upon for correction of gastrointestinal pathology. The patient also has received preoperative and/or postoperative antibiotics for prophylaxis or treatment. We can postulate that the following chain of events occurs: 1. The patient is a carrier of a virulent Staphylococcus in his nasopharynx or gastrointestinal tract which is resistant to the antibiotic being used. 2. The normal flora of the bowel is suppressed or eliminated by the antibiotic, and the resistant Staphylococcus, usually suppressed by normal bowel flora, would be allowed unrestricted growth. 3. The Staphylococcus elaborates an enterotoxin, producing severe toxicity. 4. The Staphylococcus in unrestricted growth invades the bowel wall, produces mucosal necrosis, and causes massive fluid extravasation into the bowel lumen and a severe diarrhea. 5. Fluid and electrolyte losses become massive, resulting in hypovolemia and circulatory collapse.

Evidence for the production of enterotoxin was supported by Surgalla and Dack,[36] who found its production by 30 of 33 strains of Staphylococcus isolated from patients with enteritis following treatment with antibiotics.

The disease appears most frequently in patients with gastrointestinal pathology.[26,28] In Pettet's series all involvement of the bowel was proximal to the site of the obstructing lesion in cases of carcinoma of the colon.

Attempts to produce enterocolitis in animals have failed[21]; however, a recent epidemic on chinchilla farms was found to be staphylococcal enterocolitis and was fatal to a large number of otherwise healthy animals.[40] The epidemic ceased when food pellets containing 0.2 mg. of chlortetracycline were withdrawn.

Herrell and associates[14] have suggested that the stress of surgery and release of large amounts of adrenal cortical hormones aids in development of the infection. As in any infectious disease, the course is greatly dependent upon the virulence of the organism and the resistance of the host.

Report of Cases

There have been 16 cases of staphylococcal enterocolitis on the surgical service of

TABLE 1.—*Primary Disease Present in Sixteen Cases of Staphylococcal Enterocolitis*

PRIMARY DISEASE	
Carcinoma of the colon	3
Duodenal Ulcer	3
Gastric Ulcer	2
Diverticulitis of Colon	2
Gastric Carcinoma	1
Granuloma of the Stomach	1
Acute Cholecystitis	1
Carcinoma of the Esophagus	1
Acute Appendicitis	1
Diabetic Gangrene Lt. Foot	1
Total	16

this hospital since 1953. One occurred in 1953; three, in 1954; five, in 1955, and seven, in the first six months of 1956. Two cases came to autopsy on the surgical service that presented diarrhea and shock prior to death. Autopsy revealed ulcerations in the colon, but bacterial culture from the bowel revealed only normal bowel flora despite the use of suppressive media to demonstrate Staphylococcus. Three other cases in which the clinical picture was presented and the patients survived were not bacteriologically proved and were therefore excluded. All cases were in men, who ranged in age from 40 to 77 years, with an average of 59 years. The primary disease in all but one involved the gastrointestinal tract (Table 1). One patient had diabetic gangrene of the left foot and was treated by midthigh amputation. As would be expected, other operations performed (Table 2) involved the gastrointestinal tract, and partial gastrectomy was the commonest operation.

In all but two patients the disease occurred in the postoperative period. Of these two, one was being treated for acute cholecystitis with antibiotics and developed enterocolitis on the sixth day of treatment. The other was undergoing bowel preparation with antibiotics prior to exploratory laparotomy for carcinoma of the cecum and developed the disease on the fourth day of preparation.

The disease occurred in the postoperative period from the first to the eighth postoperative day, the average being the fourth day. In 11 of the patients it occurred before the fifth postoperative day.

No common pattern of secondary disease was present in this group of patients except that 8 of the 16 patients had dental caries and pyorrhea which were not corrected prior to operation.

The following cases are considered representative and are presented in detail.

CASE 1.—A 67-year-old white man was admitted Jan. 25, 1955, with a partially obstructing carcinoma of the transverse colon. Bowel preparation was begun, using succinylsulfathiazole U. S. P., 2.0 gm. every six hours for four days, and two doses of neomycin sulfate, 1.5 gm.; each was given the day prior to operation. Partial colectomy was performed on Feb. 8. Postoperatively he was given tetracycline, 500 mg. I. V. every 12 hours.

The postoperative course was entirely normal until Feb. 15, when the patient began to have crampy abdominal pain and loose, watery stools. The temperature rose to 102 F, and the pulse rose to 110 per minute. He was given intravenous fluid in the form of 5% dextrose in isotonic saline. On Feb. 16, diarrhea increased, and he went into profound shock; the blood pressure was not obtainable, and the pulse was thready, at 140 per minute. The extremities were mottled, and cyanosis was noted. He was given 4000 cc. of 5% dextrose in isotonic saline with 40 mEq. of KCl within an hour and 2000 cc. later that day. The shock responded to this therapy, but severe diarrhea con-

TABLE 2.—*Operations Performed on Fourteen Patients Who Developed Staphylococcal Enterocolitis in the Postoperative Period*

Partial Gastrectomy	4
Partial Colectomy	2
Subtotal Gastrectomy	2
Esophagectomy	1
Appendectomy	1
Abdomino-Perineal Resection	1
Biopsy of Stomach	1
Exploratory Laparotomy	1
Midthigh Amputation	1
Total	14

tinued and the fecal loss measured 2800 cc. that day. A working diagnosis of enterocolitis was made. The tetracycline was stopped; stool culture was obtained, and erythromycin, 250 mg. I. V., was given at six-hour intervals. This drug was given for six doses and on Feb. 17 was discontinued. Chloramphenicol, 250 mg. I. V., was then administered at six-hour intervals.

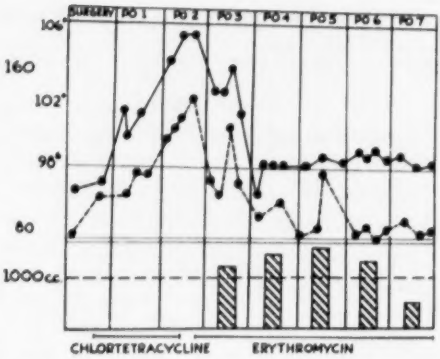
The patient was supported throughout the acute episode of enterocolitis with parenteral fluids in the form of 5% dextrose in water, 5% dextrose in isotonic saline, and sixth-molar sodium lactate. Oliguria occurred on Feb. 16, but was corrected that day and did not recur. He exhibited azotemia at the onset (NPN 59 mg. per 100 cc.), but no severe electrolyte imbalance occurred. The white blood cell count on Feb. 16 was elevated to 18,400 per cubic millimeter, with 40% segmented polymorphonuclear leukocytes and 51% stab forms. Stool culture on Feb. 16 revealed normal flora, but on Feb. 18 another revealed almost pure coagulase-positive hemolytic S. aureus, which was sensitive only to chloramphenicol and carbomycin (Magnamycin). Culture from the bowel at operation revealed no growth.

The temperature, pulse, and all signs of toxicity disappeared in 36 hours after beginning of treatment, but diarrhea persisted for eight days. The patient's course was further complicated by deep thrombophlebitis of the left leg, and he was finally discharged on April 20, 1955.

Comment.—This case demonstrates the shock that ensues from severe fluid and electrolyte loss, which was corrected by rapid administration of large amounts of fluid.

Case 2.—A 61-year-old white man was admitted Oct. 23, 1955, with recurrent massive gastrointestinal hemorrhage. Partial gastrectomy was performed on Dec. 1, 1955, for duodenal ulcer. Neomycin sulfate, 1.0 gm., and bacitracin, 25,000 units, in 100 cc. of isotonic saline were instilled into the peritoneal cavity prior to closure as a prophylactic measure. The patient was given chlortetracycline, 500 mg. I. V. every 12 hours for six doses postoperatively.

On Dec. 3, the temperature suddenly rose to 105 F, and the pulse rose to 140 per minute. He became lethargic, and the blood pressure was 80/50 mm. Hg. He complained of anorexia and mild, crampy abdominal pain (Figure). Examination revealed pharyngitis, decreased breath sounds in the right base, and distention of the abdomen, which was mildly tender to palpation. X-ray of the chest revealed atelectasis of the right lower lobe. The white blood cell count was 5000 per cubic millimeter, with 18% segmented polymorphonuclear leukocytes and 68% stab forms. Oliguria was



Diagrammatic presentation of patients' temperature and pulse taken from the chart (Case 2). Fecal losses during acute phase of enterocolitis and antibiotics are also represented.

Hatched areas represent stool output; solid line, temperature; broken line, pulse.

marked, and the NPN was 51 mg. per 100 cc. Believing atelectasis to be the cause of this picture, we performed therapeutic bronchoscopy, but, although the chest x-ray showed clearing, the symptoms and signs did not improve. On the supposition that we were dealing with enterocolitis, parenteral fluids were given and erythromycin therapy, 500 mg. I. V. every six hours, was started. Six hours after treatment was begun, a severe watery diarrhea occurred, the fecal loss being measured at 1300 to 1800 cc. during the next three days. Eighteen hours after the beginning of treatment, the temperature, pulse, and blood pressure returned to normal levels, signs of toxicity greatly diminished, and lethargy disappeared. Severe diarrhea continued for three days, and to a less degree for two more days.

The patient was given intravenous fluid to replace fecal losses on a liter-for-liter basis. Electrolytes remained near normal limits throughout, and, after 12 hours of oliguria, urinary output was maintained at about 1000 cc. per 24 hours. The NPN rose to 60 mg. per 100 cc. on the second day and then returned to normal.

Stool cultures at the onset of diarrhea revealed pure hemolytic S. aureus, which was sensitive to tetracycline, chlortetracycline, chloramphenicol, and erythromycin. Culture of secretions obtained at bronchoscopy revealed the same organisms and the same antibiotic sensitivity. The patient completely recovered and was discharged on Dec. 23.

Comment.—This case represents one in which a diagnosis was made prior to the onset of diarrhea, although atelectasis was first suspected and treated. This case does not fit the usual pattern in that the Staphy-

lococcus was sensitive to the drug (chlortetracycline) which was being administered.

CASE 3.—A 60-year-old white man was admitted to the hospital on Jan. 22. On Jan. 31 a partial gastric resection was performed for obstructing duodenal ulcer. The patient was given oxytetracycline, 100 mg. I. M. every six hours (total dose was 0.6 gm.).

On the morning of Feb. 2 the patient's temperature rose to 102.6 F, and later to 104 F. The pulse increased to 136 per minute, and the blood pressure was 86/70 mm. Hg. He complained of abdominal cramping pain, and examination revealed right upper quadrant tenderness with some rebound tenderness. Hypoactive bowel sounds were present, and the abdomen was distended. The patient was lethargic and responded to questioning poorly. By evening, abdominal distention and tenderness had increased, and there was some rigidity to palpation. Laboratory studies revealed low serum sodium (130 mEq/L.), serum chlorides 95 mEq/L., and the white blood cell count 2500 per cubic millimeter, with 13% segmented polymorphonuclear leukocytes and 63% stab forms.

Enterocolitis was strongly considered, but because a leak of the duodenal stump or anastomosis could not be ruled out, exploratory laparotomy was done. The duodenal stump and anastomosis was intact, but the entire small bowel was diffusely distended, atonic, edematous, and hyperemic. The bowel was filled with fluid, and a trochar enterotomy was performed to facilitate closure of the abdomen. Thirty-five hundred cubic centimeters of plasma-like fluid was removed, which on direct smear showed large numbers of Gram-positive cocci, substantiating the diagnosis of enterocolitis, and treatment was begun.

Erythromycin, 500 mg., and chloramphenicol, 500 mg., were given I. V. immediately, and erythromycin, 250 mg., was administered I. V. at six-hour intervals. Cortisone was given, 50 mg. I. M., after surgery and in decreasing doses daily for four days. He was given 5000 cc. of intravenous fluid on Feb. 2, which included 1 unit of blood and 1 unit of dextran. Seven thousand cubic centimeters was given on Feb. 3, of which 4500 cc. was in the form of 5% dextrose in isotonic saline. Blood pressure remained at hypotensive levels for 36 hours, and oliguria occurred immediately but was corrected within 36 hours. Electrolytes returned to near normal within 48 hours. The NPN rose to 83 mg. per 100 cc. on Feb. 5 and then returned to normal. On Feb. 5 the white blood cell count was 6400, with 24% segmented polymorphonuclear leukocytes and 64% stab forms. The differential count returned to normal within three days.

The temperature, pulse, and clinical evidence of toxicity responded to treatment in 48 hours. Diarrhea did not occur until Feb. 5, was mild, and lasted only two days. Culture of the bowel fluid obtained at operation revealed pure hemolytic S. aureus, which was sensitive to chlortetracycline, chloramphenicol, erythromycin, and streptomycin. On Feb. 10 stool culture revealed the same organism, now resistant to all antibiotics. On Feb. 6 wound separation occurred, resuturing was done, and healing followed. The patient was discharged on April 6, 1956.

Comment.—This patient presented a picture compatible with enterocolitis, but the abdominal symptoms increased and an intra-abdominal catastrophe could not be ruled out without exploration. The laparotomy presented an opportunity to view the bowel of enterocolitis.

In our group of patients, 12 of 16 received preoperative antibiotics in the form of neomycin, bacitracin, penicillin, or streptomycin, singly or in combination with chemotherapeutic agents, such as succinylsulfathiazole or phthalylsulfathiazole, usually administered as a bowel preparation. Tetracycline was administered therapeutically to two patients; erythromycin, to one, and penicillin, to one; and in each case sensitivity tests of the Staphylococcus isolated from stool culture showed resistance to the antibiotic.

Two patients received intraperitoneal neomycin and bacitracin at operation, but sensitivity tests were not performed at any time on these two drugs.

TABLE 3.—*Antibiotics Administered in the Postoperative Period to Sixteen Patients Who Developed Staphylococcal Enterocolitis*

Postoperative Antibiotics	Number of Patients Treated	Staphylococcus	
		Resistant	Sensitive
*Tetracycline	7	7	0
Chlortetracycline	3	2	1
Oxytetracycline	1	1	0
**Penicillin	2	2	0
Penicillin & Strep.	2	2	0
Streptomycin	1	1	0
Total	16	15	1

*Includes 1 patient not operated who received tetracycline in treatment of cholecystitis.
**Includes 1 patient who received penicillin in a bowel prep.

Postoperative antibiotics were administered to all 16 patients (Table 3). All staphylococci isolated from stool culture after onset of enterocolitis were resistant to the antibiotic being used in the postoperative period, except in one case, in which chlortetracycline was given (Case 2). The antibiotics administered for treatment and bowel preparation in the two nonsurgical cases are included in this group, and in both the pathogen was resistant.

The symptoms and signs present in the entire group are tabulated in Table 4. Diarrhea, clinical evidence of toxicity, and temperature elevation were the most consistent findings. Shock occurred in 8 of 16 cases.

Stool cultures were performed in all cases. In four cases blood cultures were done at the onset of the disease and all were negative.

The antibiotic sensitivity of the 16 strains are listed in Table 5. No pattern of sensitivity was established except that 14 of the 16 strains were sensitive to chloramphenicol. The two strains showing resistance to this drug occurred in 1956.

Daily measured fecal losses ranged from 1000 to 6000 cc. in 24 hours. Oliguria occurred in eight patients at the onset or on the second or third day of the disease.

Electrolyte imbalance occurred in 10 patients and was severe in 5. This was always corrected in 48 hours or less.

Azotemia was present in 7 of 11 cases recorded (NPN 50 to 90 mg. per 100 cc.).

TABLE 4.—*Symptoms and Signs in Sixteen Patients with Enterocolitis*

Symptoms & Signs	Present In	Severe	Moderate	Mild
Diarrhea	16	8	5	2
Toxicity	14	6	6	2
Abdominal Distention	12	3	4	5
Abdominal Pain	9	3	2	4
Nausea & Vomiting	8	0	4	4
Shock	8	6	2	0
Temperature Elevated	15	6	9	0
Pulse Elevated	15	6	9	0

TABLE 5.—*Antibiotic Sensitivity of Strains of Virulent Hemolytic Staphylococcus Aureus Isolated in Stool Cultures of Sixteen Patients with Enterocolitis*

Antibiotic	Resistant	Sensitive
Tetracycline	14	2
Chlortetracycline	12	4
Oxytetracycline	14	2
Chloramphenicol	2	14
Erythromycin	10	6
Magnamycin	6	4*
Penicillin	12	4
Streptomycin	14	2

*Sensitivity study on magnamycin in only 10 cases.
All studies performed with Difco Disks. Pen. 1 u/ml, Strep. 10 mcg/ml, Eryth. 1 mcg/ml, Magna. 1 mcg/ml, Chlortetracycline, Oxytetracycline, Tetracycline, and Chloramphenicol = 10 mcg/ml.

The white blood cell count was recorded in nine, was elevated in five, and was normal or below normal in four. All differential counts showed a marked shift to the left.

Durations of fever and toxicity ranged from 12 to 72 hours and averaged 48 hours.

Treatment was begun in 12 of the 16 cases within 24 hours of the onset of presenting symptoms.

The diagnosis was made and treatment instituted prior to onset of diarrhea in six of the cases. When diarrhea occurred, the direct smear of the stool was utilized in most cases and proved a valuable adjunct for diagnosis.

Antibiotic treatment of enterocolitis consisted of erythromycin and chloramphenicol in 13 cases, erythromycin in 2 cases, and erythromycin and penicillin in 1 case.

Fluid replacement for electrolyte and fluid loss was based on measured loss, the response of the patient, and measured urinary output. In all patients we attempted to achieve a 1000 cc. output per 24 hours.

The response of symptoms in time was variable. Diarrhea resolved in 48 hours to 10 days, and in all but four cases responded to treatment within 96 hours. Only one patient had hypotension longer than six hours.

Comment

In reviewing these cases, several factors were noted which would incriminate cross

infection as an important consideration in this disease. The patients were hospitalized in open surgical wards. The stay in the hospital prior to onset of enterocolitis was found to average 35 days. Of 16 patients, 12 were hospitalized over two weeks and 10 over three weeks. The transfer of resistant staphylococci from hospital personnel to patients and from patient to patient has been well documented.[22,33,34] Todd,[35] in 1955, did bacteriologic studies on all patients and the staff of a hospital ward after two consecutive cases of enterocolitis occurred which terminated fatally. Seven patients and one staff member were found to be carriers of 17 strains of virulent S. aureus. Seven of these were found to be of the same phage type and sensitivity as the organism causing the enterocolitis. The staff member carried the lethal strain.

Cairns[3] found an increase from 25% to 68% of resistant strains of Staphylococcus in the nasopharynx of patients hospitalized from one to eight days. In some cases of enterocolitis, staphylococci with the same antibiotic sensitivity have been isolated from stool and sputum cultures[16,37] and from stool and vomitus cultures.[16,18] It has also been suggested that the resistant Staphylococcus may be carried to the gastrointestinal tract by Levin tubes.[4] Poor oral hygiene and dental caries were present in eight of our patients, conditions which certainly provided a fertile ground for the organism.

The prerequisites for development of staphylococcal enterocolitis are (1) bowel pathology, (2) suppression of normal bowel flora with antibiotics, (3) overgrowth of resistant Staphylococcus, and (4) cross infection as the source of the pathogen.

Prophylaxis should properly be directed at prevention of cross infection and intelligent use of bacteriologic studies as a guide to antibiotic administration. Control of cross infection would be best obtained by isolation technique in caring for patients with staphylococcal infections. Careful handling of dressings and observation of basic rules governing care of infected wounds are an absolute necessity. Increasing resistance of the Staphylococcus to all antibiotics should bring about renewed interest in this neglected facet of surgical care.

Patients undergoing major surgery, especially elective gastrointestinal surgery, should have foci of infection eliminated prior to operation. Also, nasopharyngeal culture with antibiotic sensitivity studies prior to operation will serve as a guide to antibiotic preparation or therapy if a resistant Staphylococcus is found. Culture of the bowel fluid at operation and the finding of a resistant Staphylococcus alerts the physician to the first signs of the disease, and early treatment can be instituted.

The value of the Gram-stained fecal smear in a patient who exhibits diarrhea in the postoperative period cannot be overemphasized. A few staphylococci are common in the feces, but a predominance of Gram-positive cocci in the smear warrants treatment without waiting for a culture. Treatment should be directed along four major lines.

1. The antibiotic being used is withdrawn.
2. Treatment with the antibiotic which currently exhibits the greatest Staphylococcus sensitivity is begun.
3. Parenteral fluids and electrolytes are given in relatively large amounts immediately and blood or plasma expanders as indicated.
4. The patient's treatment is supervised closely and continuously.

We believe that early diagnosis and early adequate treatment will reduce the mortality.

Conclusions

Most cases of enterocolitis are due to an antibiotic-resistant, virulent hemolytic S. aureus.

There is a definite increase in the number of cases of staphylococcal enterocolitis, which is coincident with the increasing resistance of the Staphylococcus to antibiotics.

Early diagnosis and early, adequate treatment will result in reduction of the mortality rate.

Prophylactic measures, such as control of cross infection and judicious use of antibiotics, guided by bacteriologic studies, will reduce the incidence of the disease.

Summary

This paper presents a review of 16 cases of staphylococcal enterocolitis, in all of which the patients survived. Three cases are presented in detail. The pathogenesis of the disease is discussed, especially in relation to cross infection and antibiotic therapy. Early diagnosis and treatment are advocated to bring about reduction in mortality. Suggestions for prevention of the disease are presented.

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DISCUSSION

DR. JOHN VAN PROHASKA, Chicago: The authors have given a fine presentation of a well-organized paper. I wish to congratulate them on their successful treatment of 16 cases of staphylococcal enterocolitis without a death.

In this serious disease, a given treatment does not entirely reflect the effectiveness of the therapeutic measures. I should like to emphasize that the 100% survival in this series reflects to a large measure the degree of virulence of the Staphylococcus and, particularly, the degree of toxicity of the enterotoxin produced by the particular strain of Staphylococcus.

Experimental evidence points out that different strains of staphylococci will produce enterotoxin of different degrees of toxicity, and will produce the enterotoxin in different amounts. In like manner, some cases of pseudomembranous enterocolitis are very severe and almost always fatal, whereas others are very mild and respond to any simple therapeutic measure. The pseudomembranous enterocolitis observed within the past four years has been much less severe than that observed in the earlier cases.

We have published enough clinical evidence to point out that corticotropin has a remarkable effect on pseudomembranous entercolitis. We have given corticotropin to some 18 patients and have observed that the symptoms of diarrhea, toxemia, fever, and leukocytosis disappeared usually within 24 hours and the patient returned uneventfully to a normal state. We have also accumulated experimental evidence that kittens extremely sensitive to enterotoxin manifest no reaction when they are prepared with intramuscular doses of corticotropin. Lastly, we have shown that when enterotoxin is given to dogs that are highly resistant to its toxic effects, it will produce physical changes in the small bowel suggestive of enteritis.

DR. EDWARD S. JUDD, Rochester, Minn.: In 1954 my colleagues and I published a paper in *Surgery, Gynecology and Obstetrics* on pseudomembranous enteric disease. This stimulated Dr. Prohaska, at the Seattle meeting of the Western Surgical Association, to invite me to discuss his very fine paper there, since we had made the statement in our paper that the incidence of pseudomembranous enteric disease has not changed much at our institution during the years. We were referring, of course, to the particular entity described so beautifully by John M. T. Finney long before the turn of the century—long before sulfonamide compounds, antibiotic agents, and similar aids became available. At the time we made our statement we had the feeling that there are in fact several similar entities, and I am glad to hear Dr. Prohaska report that there may be variations of similar phenomena.

In the presence of pseudomembranous enteric disease we have found no specific organism that we can demonstrate by culture, even though we resort to the use of the most modern and efficient

of all the culture media, and even though we make use of all the inhibitors which the bacteriologists have been able to devise. Unfortunately, pseudomembranous enterocolitis which does not have a basis in invasion by micrococci continues relentlessly to take its victims to the grave, in spite of all therapy we have been able to investigate or to devise ourselves, and that includes the use of corticotropin and cortisone.

DR. MILES SMITH, Milwaukee: I should like to stress just one point that Dr. Lepley raised, which we did not have time properly to emphasize and which seems pertinent to the discussers' comments.

The question immediately arises, "Where does the patient get this infection? Must we assume this is beyond our control?" Apparently that is not entirely so. Last fall we set out to determine just how many of our surgical patients were carriers. We found that from 7% to 10% of the patients admitted to the general surgical sections of our hospital had this virulent organism in the nasopharynx at the time of their admission; but, more important, we found that within 10 to 14 days following admission approximately 40% of these patients had become nasopharyngeal carriers. Our attention was then turned toward our own staff, and by nasopharyngeal and anal cultures it was found that approximately 50% of the physicians, nurses, and attendants in the operating rooms and on the wards were carrying these virulent strains of staphylococci in the nasopharynx or the bowel or both.

It has repeatedly been demonstrated that the long-term hospital case is often contaminated by his environment in the hospital, but this study brings out with great clarity the part played by our professional staff in acting as a reservoir for this pathogen.

Because these organisms demonstrated great resistance to the tetracycline group, we have recently embarked on a hospital-wide experiment of shelving this group of antibiotics for a four-month period to see whether putting them on the shelf would decrease the incidence of resistance of this organism to the antibiotic. It has been gratifying to see a definite favorable trend in the cultures taken monthly from all surgical personnel so far.

If the outcome of this study is favorable, on the basis of presumptive evidence to date, we shall consider rotating our antibiotic drugs, always having one on the shelf to preserve its therapeutic effect and to lessen the hazard of staphylococcal enterocolitis in the patient who must undergo gastrointestinal surgery.

It has been very rewarding to note the immediate effect of our study in our own surgical service. As Dr. Lepley has said, in the first six months of 1956 there were seven cases of staphylococcal enterocolitis, but since July, 1956, there has been only one case. This reflects our greater awareness of the hazard of the unwise use of antibiotics before and after surgery, and a much more intelligent use of bacteriologic sensitivity examinations.

We could not, of course, have done any of this without a tremendously devoted bacteriologic staff.

DR. WILLIAM A. ALTEMEIER, Cincinnati: This will be the first time I have ever discussed a paper which I have not read or heard. I have just had a long-distance telephone call, and I am sorry I did not hear the presentation. (Laughter)

At the request of our president, I arise to discuss this paper, and I shall be glad to give some of my ideas in regard to this subject based upon the abstract of the paper which appears in the program.

The first thing we should realize is that this infection is just as apt to occur in the absence of antibiotic therapy as it is as a complication of antibiotic therapy. Persons who harbor this resistant strain of the hemolytic S. aureus may become victims of this infection if circumstances permit the organism to proliferate in the intestinal tract uninhibited by other bacteria present or stimulated by some other factor.

The carrier state with the Staphylococcus is well known. A symposium in Washington on Oct. 18, 1956, was devoted to a consideration of the problems presented by resistant staphylococci.

It is my impression that all staphylococci cannot produce pseudomembranous enterocolitis. Those producing an enterotoxin have a necrotizing action on the mucosa of the intestinal tract and are particularly prone to be the causative agent.

At the present time we are reviewing all of the cases of pseudomembranous enterocolitis caused by the Staphylococcus in our area, at the request of the Food and Drug Administration. It is interesting to note that approximately half of these have not had antecedent antibiotic therapy.

I note that in the outline the questions of hypovolemia, circulatory collapse, and shock are stressed. In the shock which occurs with this condition in our experience, the blood pressure has fallen as the temperature and white blood cell count have risen. It has not been uncommon to see rises of temperature to 105 or 107 F or more and an associated fall in blood pressure to levels of 60 mm. Hg or less.

Hypovolemia may be, and undoubtedly is, the cause of shock in some of these instances, but I think more important in this type of shock is a disparity between the normal, or nearly normal, circulating blood volume and the vasodilation in the peripheral circulation. In other words, there is a disparity between the blood volume and the capacity of the peripheral bed which permits the patient suddenly to bleed into his dilated peripheral

bed. This has the same effect, of course, as hypovolemia.

Other causes appear to be toxic effects of the bacterial toxins on the myocardium and toxic or hemorrhagic changes in the adrenal gland.

Because of the incidence of a disparity between the normal blood volume and the increased peripheral vascular bed, it is easy to throw patients with this condition into pulmonary edema if fluids are infused rapidly. It has been our experience in some instances that the use of fluids has failed to produce any significant response in blood pressure unless levarterenol (Levophed) is used. For this reason the use of levarterenol is now routine in the management of these patients for the purposes of raising the blood pressure to about 80 mm. Hg, of maintaining a urinary filtration pressure, and of ensuring the vital activity of the brain, liver, and other organs.

One final word about this organism. In the majority of instances in our area it has been very susceptible to erythromycin and chloramphenicol. Between 90% and 100% of the staphylococci in the Cincinnati area have been and still are sensitive to chloramphenicol. In the event that erythromycin is not effective in the treatment of a patient with staphylococcal pseudomembranous enterocolitis, chloramphenicol should be used.

DR. DERWARD LEPLEY JR., Wood, Wis.: In answer to Dr. Judd, I realize that we must differentiate between this disease and pseudomembranous enterocolitis. What we are talking about is a specific entity. I know that we do not have the answer to the cause of pseudomembranous enterocolitis, though many theories of etiology are recorded in the literature.

With regard to Dr. Altemeier's question of hypovolemia: We feel very strongly about fluid replacement. To cite one example, we found a patient in shock on the third postoperative day following gastrectomy. He received 6 liters of isotonic saline within an hour, and his blood pressure was restored to normal levels. He did not evidence shock again and was extremely toxic at the time.

In another case we made the mistaken diagnosis of ruptured duodenal stump and the patient was reexplored, although we were thinking of enterocolitis at the time. He was extremely toxic, and at operation he was found to have the entire small bowel filled with a plasma-like fluid, which upon removal with suction was found to be about 4000 cc.

These are just two observations which support the occurrence of marked hypovolemia.

Management of Symptomatic Aganglionic Megacolon in Early Infancy

WILLIAM K. SIEBER, M.D., and BERTRAM R. GIRDANY, M.D., Pittsburgh

Aganglionic megacolon is an important and frequent cause of intestinal obstruction in neonatal and young infants. Its clinical recognition and treatment warrant further evaluation. This paper reviews the recent experience at the Children's Hospital of Pittsburgh in 30 infants with symptomatic aganglionic megacolon. The data show the serious nature of the condition and indicate that prompt colostomy to relieve obstruction must take precedence over medical and drug therapy.

Literature

In 1952, Potts, Boggs, and White [1] reported their experience in 10 young infants with symptomatic aganglionic megacolon. Six of these infants died. The authors concluded that an early pull-through procedure was indicated but that sigmoid colostomy was the procedure of choice in the poor-risk infant. Ehrenpreis [2] recorded his observations in 10 infants with symptomatic aganglionic megacolon; 5 infants died. Hays and Norris [3] reported a mortality rate of more than 50% in infants hospitalized in the neonatal period for obstruction due to aganglionic megacolon. Swenson and Fisher [4] reviewed their experience with Hirschsprung's disease in infancy and observed the highest mortality rate in the youngest age group. They emphasized the need for rectal biopsy to establish the diagnosis and recommended that colostomy be done as soon as the diagnosis was established. Klein and Scarborough [5] reviewed their experience with five infants. Moriarty and Ramsey [6] described pseudomembranous colitis complicating symptomatic aganglionic megacolon in early infancy.

Material

Thirty infants with symptomatic aganglionic megacolon were admitted to the Children's Hospital of Pittsburgh during the past six years. There were 5 female and 25 male infants. One infant was Negro. His sibling was admitted at 2 years of age with proved aganglionic megacolon. This was the only known instance of familial disease.

All infants were the products of full-term gestation and had normal birth weights. Histologic examination substantiated the diagnosis of aganglionic megacolon in all cases. Seventeen infants were admitted to the hospital before they were one month of age. In two female infants ganglion cells were absent from the terminal ileum and entire colon. In 6 infants the aganglionic area extended from the anus to the transverse colon; in the remaining 22 infants the aganglionic area extended from the anus to various levels in the rectum and sigmoid colon. One infant had accompanying malformations of the intestinal tract, consisting of ileal stenosis and malrotation of the midintestine with obstructing duodenal bands. One infant was Mongoloid. None of these 30 infants had associated genitourinary anomalies.

Clinical Course

The term symptomatic aganglionic megacolon applies to those infants admitted to the hospital because of severe constipation with episodes of complete intestinal obstruction, complete intestinal obstruction at birth, or intermittent partial intestinal obstruction. This report does not concern itself with infants in whom obstipation is the only

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From the Departments of Surgery and Radiology, Children's Hospital of Pittsburgh and the University of Pittsburgh School of Medicine.

TABLE 1.—*Clinical Course and Results in Thirty Infants*

Clinical Course	No.	Living	Died
Constipation with obstruction	8	7	1
Complete obstruction at birth	13	8	5
Intermittent obstruction	9	3	6
Total	30	18	12

major problem; in this group periodic abdominal distention occurs, weight gain is poor, and fecal impactions are common.

In the group under study, eight infants had a history of obstipation with gradually increasing abdominal distention. They had recurrent bouts of respiratory infection and were chronically ill. Each had one or more episodes of complete intestinal obstruction, partially relieved by enemas.

Complete intestinal obstruction was present at birth in 13 infants. They had abdominal distention, vomited bile, and did not spontaneously pass meconium. One infant had pneumoperitoneum secondary to perforation of the cecum. Roentgen signs of meconium peritonitis indicated that three infants had had antenatal intestinal obstruction and perforation.

Nine infants had intermittent partial intestinal obstruction. They passed meconium but developed gradually increasing abdominal distention in the neonatal period. They nursed poorly, and their bowel movements were scanty. Enemas produced temporary relief of symptoms. They failed to gain weight normally. Suddenly, often within hours, they became seriously ill with respiratory distress and gross abdominal distention.

Results

Of 30 infants, 18 survived and 12 died (Table 1). The one death in the group of eight who had obstipation and episodes of acute intestinal obstruction occurred in an infant with aganglionosis of the entire colon. Of 13 infants with complete obstruction at birth, 5 died. Their deaths were associated with colitis in two instances; technical surgical errors contributed to the deaths of three other infants. Of the nine infants with intermittent severe obstruction, six died. The deaths were associated with technical surgical error in one, inanition in three, and phlegmonous colitis in two, infants.

Tables 2 and 3 summarize the necropsy findings. Two infants had phlegmonous, and two pseudomembranous, colitis. In five infants death was associated with errors of technique, either in the performance or in

TABLE 2.—*Summary of Deaths*

No.	Age When First Seen	Delay Before Surgery	Operation	Findings at Necropsy	Comment
1	3½ mo.	10 days	Transverse colostomy	Phlegmonous colitis	Methacholine 8 days; operated upon *in extremis;* died 4 hr. P. O.
2	9 days	11 days	Sigmoid colostomy	Phlegmonous colitis	Died 2 days P.O.
3	7 days	4 hr.	Sigmoid colostomy	Pseudomembranous colitis	Died 3 days P.O.
4	7 days	3 hr.	Sigmoid colostomy	Pseudomembranous colitis	Died 6 hr. P.O.
5	2 mo.	3 mo.	Transverse colostomy	Chronic pyloric obstruction; malnutrition	Partial evisceration 4th P.O. day; died 30th P.O. day
6	3 days	3 days	Appendicostomy; closure appendicostomy 8 days later; transverse colostomy age 6 wk.	Unrelieved colonic obstruction; malnutrition	Died 2 days after colostomy
7	5 mo.	3 hr.	Laparotomy; 10 days later ileotomy and ascending colostomy	Unrelieved obstruction; peritonitis	Aganglionosis of entire colon and terminal ileum; died 5 days P.O.
8	12 days	3 days	Transverse colostomy	Peritonitis	Perforation of proximal colon by tube in colostomy; died 6 days P.O.
9	5 days	1 day	Pull-through procedure	Unrelieved obstruction; peritonitis	Insufficient aganglionic colon removed; peritonitis secondary to rectal tube perforation preoperatively
10	1 mo.	3 days	Transverse colostomy	Inanition; sclerema	Evisceration 5th P.O. day; died 6th P.O. day
11	2 mo.	2 days	Transverse colostomy	Inanition	Died 3d P.O. day
12	2 mo.	1 day	Transverse colostomy	Inanition	Evisceration 5th P.O. day; evisceration 10th P.O. day; died 20th P.O. day

TABLE 3.—*Major Necropsy Findings in Twelve Infants*

Colitis		4
Pseudomembranous	2	
Phlegmonous	2	
Inanition		3
Unrelieved obstruction		3
Peritonitis (perforation by catheter)		1
Pyloric obstruction secondary to partial evisceration		1
Total		12

the choice of the operative procedure. One infant had partial evisceration with subsequent pyloric obstruction. In two instances the colostomy had been placed in the aganglionic colon and failed to relieve obstruction. Peritonitis was present in two infants. Three infants had inanition and starvation following prolonged chronic colonic obstruction.

Table 4 summarizes the data concerning the 18 infants who survived. Three infants, after many hospital admissions for fecal impactions, pneumonia, and intestinal obstruction, had primary pull-through procedures, at 20 months, 21 months, and 3 years of age, respectively. Each of these patients had a good clinical result. None had an operative procedure during his hazardous early life. One infant with aganglionosis extending from the anus to the splenic flexure was deliberately not subjected to colostomy because of the expected difficulties of later definitive surgery. It was presumed that the mesocolon would become inadequate in length to permit a later pull-through procedure. In this infant a primary pull-through procedure was carried out at 7 months of age. Insufficient aganglionic colon was removed, and he still requires enemas.

Appendicostomy relieved acute obstruction in one 17-day-old infant. He had repeated episodes of fecal impaction from 6 weeks of age until a successful pull-through procedure was done, at 4½ years of age. One infant required laparotomy at 7 days of age for correction of associated malrotation and ileal stenosis. He had an excellent result following a pull-through procedure at 21 months of age.

In one 5-day-old infant, collapsed distal ileum was misinterpreted at laparotomy as ileal stenosis, and a right colectomy was done. The absence of ganglion cells in the resected colon reported by the pathologist established the diagnosis of complete agan-

TABLE 4.—*Summary of Survivals*

No.	Surgery	Age at Surgery	Delay	Postoperation Complications	Present Status	Comment
1	None				Pull-through at age 21 mo.	Well
2	None				Pull-through at 3 yr.	Well
3	None				Pull-through at 20 mo.	Well
4	Transverse colostomy	8 days	5 days	Ascites	Awaiting definitive surgery	
5	Transverse colostomy	6 days	3 days	Enterocolic fistula	Pull-through at 9 mo.	Fair result, aganglionic intestine remains
6	Transverse colostomy	6 wk.	17 days	None	Pull-through at 13 mo.	
7	Transverse colostomy	8 days	2 hr.	Acute appendicitis 5 days P.O.	Awaiting definitive surgery	
8	Transverse colostomy	24 hr.	2 hr.	None	Pull-through at 13 mo.	Stricture at anastomosis—poor result
9	Sigmoid colostomy	6 wk.	1 day	Incisional abscess	Awaiting definitive surgery	
10	Sigmoid colostomy	6 days	3 hr.	None	Awaiting definitive surgery	Emergency colostomy, perforation of rectum by tube
11	Sigmoid colostomy	8 days	4 hr.	None	Pull-through at 13 mo.	Died 8 days P.O. Mongolian
12	Sigmoid colostomy	11 days	2 hr.	None	Pull-through at 16 mo.	
13	Sigmoid colostomy	7 mo.	2 mo.	Evisceration 5th P.O. day	Pull-through at 3 years	
14	Sigmoid colostomy	2½ mo.	12 hr.	None	Pull-through at 16 mo.	Mild prolapse of colostomy
15	Pull-through	7 mo.	2½ mo.	None	Constipated	Insufficient intestine removed
16	Appendicostomy	17 days	24 hr.	None	Pull-through at 4½ yr.	Well
17	Laparotomy; Ladd procedure; anastomosis for ileal stenosis	7 days	2 hr.	None	Pull-through at 21 mo.	Well
18	R. colectomy	5 days	3 days		Emergency ileostomy at 1 mo.; ileorectostomy at 6 wk.	Died at 11 mo.

glionosis of the colon. At one month of age complete obstruction recurred, necessitating ileostomy. Ileorectostomy at 6 weeks of age was followed by breakdown of the suture line, septicemia, panosteomyelitis, and death from inanition at 11 months of age.

Of the remaining 11 infants, 6 had sigmoid, and 5 transverse, colostomies. These colostomies were done as emergency procedures in all but two infants. Postoperative complications included enterocolic fistula in one, acute appendicitis on the fifth postoperative day in another, evisceration in a third, and incisional abscess in a fourth, infant.

Decompression following colostomy was complete within three days, and clinical recovery was rapid. The usual hospital stay following colostomy was three weeks.

Of these 18 infants, 16 have thrived. Twelve have had pull-through procedures, and four are awaiting definitive surgery. The Mongoloid infant did well following colostomy at 8 days of age, but died after a pull-through procedure at the age of 13 months. One infant with complete aganglionosis of the colon died at 11 months of age, following ileorectostomy at 6 weeks of age.

Diagnosis

Aganglionic megacolon is suspected in any infant with signs of complete or partial low intestinal obstruction. Progressive abdominal distention and scanty stools are present. Paradoxical diarrhea around fecal impaction occurs. Foul-smelling, frequent stools are an ominous sign, indicating phlegmonous colitis.

The roentgen examination usually allows definitive diagnosis. The lateral film of the abdomen shows a tiny-calibered, air-containing rectum (Figs. 1 and 2); dilated loops of air-containing bowel distend the the abdominal cavity. In 27 of the 30 infants plain film examinations suggested the correct diagnosis.

Figs. 1 and 2.—Posteroanterior and lateral erect films of the chest and abdomen of a 5-day-old infant show free air under the diaphragm. The tiny-calibered, air-containing rectum is well visualized in the lateral view. There is sharp transition to the dilated, normally innervated bowel.

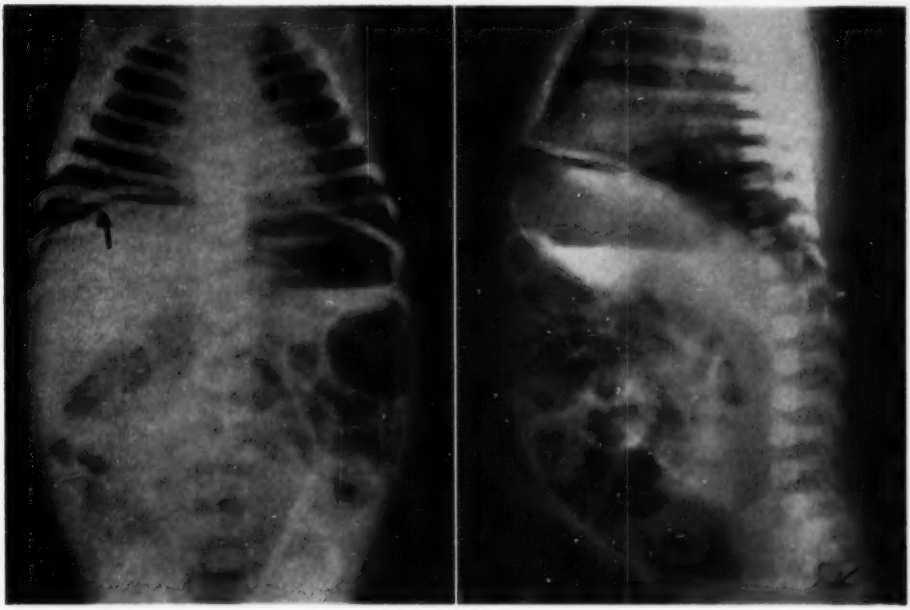

Fig. 3.—A contrast medium study in the same infant (Fig. 2) shows the same changes.

Fig. 4.—Lateral film of the abdomen in a 7-day-old infant with diarrhea, shock, and foul-smelling stools shows ulcerative changes in the colon. The colon is not dilated.

Opaque studies define the caliber of the distal colon and the site of transition to dilated bowel (Fig. 3). These examinations are carried out with Dionosil*-saline mixtures introduced by gentle pressure of a hand syringe through a soft-rubber catheter, with its tip inserted into the distal rectum. The contrast studies help the surgeon to plan his operative procedure, particularly with reference to the colostomy site. Introduction of this water-soluble opaque material in saline suspension is a safe, rewarding procedure. The use of barium mixtures is contraindicated; barium becomes inspissated and adds to the obstruction. Plain film examinations and opaque studies afforded rapid, accurate diagnosis of aganglionic megacolon in 27 of these 30 infants.

X-ray examinations were not diagnostic in the two infants with aganglionosis of the entire colon and terminal ileum. One infant (Figs. 4 and 5) with severe diarrhea showed the roentgen changes of ulcerative colitis. His colon was not large, and he did

Fig. 5.—Necropsy specimen shows the gross changes of pseudomembranous colitis.

* Dionosil (aqueous suspension) is the *n*-propyl ester of 3,5-diiodo-4-pyridone-N-acetic acid.

not have signs of intestinal obstruction. Rectal biopsy established the diagnosis of aganglionic megacolon. This infant, at necropsy, had phlegmonous colitis and achalasia of the distal rectum. Rectal biopsy requires general anesthesia and implies a therapeutic delay until histologic examination is possible.

The differential diagnosis of symptomatic aganglionic megacolon in early infancy includes all causes of low intestinal obstruction, tracheoesophageal fistula without esophageal atresia,[7] celiac disease, and primary peritonitis.

Comment

"Conservative" or medical management of megacolon utilizes drugs, enemas, and wetting agents. Drugs which increase peristaltic activity proximal to the site of obstruction promote the development of colitis and do not relieve obstruction. Repeated enemas are dangerous. The aganglionic distal colonic segment has a thin, easily perforated wall. Actual perforation of the rectum did occur in four infants. The known dangers of water intoxication from enemas in older infants and children with megacolon[8,9] imply a similar danger in young infants with the disease.

The high mortality rates recorded in the treatment of aganglionic megacolon in young infants indicate that the approach to the problem must be more aggressive. Prompt surgical intervention to relieve obstruction takes precedence over poorly founded attempts at medical therapy.

Experience at the Children's Hospital of Pittsburgh illustrated the evolution and validity of these concepts. Prolonged nonsurgical treatment rarely accomplished lasting improvement after the infant with aganglionic megacolon experienced an episode of intestinal obstruction. Rather did "conservative" management lead to a state of chronic colonic obstruction, inanition, and severe malnutrition. Subcutaneous fat disappeared; recurrent pulmonary infec-

Fig. 6.—Plain films of the abdomen of a 6-week-old infant with obstipation and intermittent complete intestinal obstruction show the narrow-calibered rectum and distal colon without signs of intestinal obstruction.

Fig. 7.—Plain film of the abdomen of the same infant after four days of "medical" treatment shows characteristic signs of intestinal obstruction and a markedly dilated colon. No air is present within the rectum. The distention occurred suddenly.

tions developed, and phlegmonous colitis supervened. Surgery had little to offer after the obvious failure of medical regimens. Moreover, prolonged medical therapy to prepare the infant for surgery did not accomplish its purpose (Figs. 6 and 7). The fact emerged that the infant with intestinal obstruction would never be in better condition for surgery than he was at that time; further delays and medical regimens interfered with, rather than improved, his chances of survival.

The data support these conclusions. The highest death rate occurred in those infants who had intermittent intestinal obstruction. Six of the nine infants in this group died following medical regimens and prolonged attempts to improve their condition prior to surgery. Two infants who presented with complete intestinal obstruction at birth developed phlegmonous colitis after medical management elsewhere and died within hours after admission. Six of the eight surviving infants in this group were subjected to emergency colostomy.

Prejudice against and misinformation about colostomies were gradually eliminated. Many pediatricians had believed that the operative procedure was excessively dangerous, and subject to complications. They regarded colostomies as injurious to the infants' health and as difficult to manage. The care of the colostomy affords little more trouble than the usual diaper changes in normal non-toilet-trained infants. Transverse colostomies and those performed just proximal to the site of aganglionosis do not interfere with nutrition. Ascending colostomies may pose a problem in fluid and electrolyte balance.

Evisceration occurred after colostomy in five infants, two of whom died. Revision of the usual technique of colostomy prevents this complication. The placement of a rod under the exteriorized loop of colon to allow the abdominal wall to adhere to this loop is an inadequate method in a young infant and predisposes to evisceration. Because of the huge size of the distended colon, the surgeon must make the opening in the abdominal wall snug about the intestine and must decompress the colon at the time of operation. The bowel is exteriorized through a left muscle-splitting incision in the sigmoid area or through a muscle-splitting left rectus incision for transverse colostomy. An opening is made in the mesocolon at the colostomy site. The peritoneum and each successive layer of the abdominal wall are sutured beneath the loop of exteriorized colon. Peritoneum, fascia, and skin are sutured to the serosa to prevent evisceration. After exteriorization, a purse-string suture is placed in the apex of the exteriorized bowel and suction applied; a mushroom catheter is left in place. The colostomy is opened two to three days later, using the cautery.

Transverse colostomies may prevent recognition of the site of transition from aganglionic to normally innervated bowel

at later surgery. They also create the necessity of two operative procedures in future definitive surgical treatment. Moreover, the mesentery supplying the bowel distal to the colostomy site becomes shortened. Colostomy 2 or 3 in. (5 or 7.5 cm.) proximal to the site of transition avoids these complications. Biopsy at the colostomy site establishes the presence of ganglion cells in the absence of an obvious site of transition.

Summary and Conclusions

The experience in 30 young infants with symptomatic aganglionic megacolon is reviewed.

Roentgen studies using lateral films of the abdomen enable clinical recognition of aganglionic megacolon in early infancy. Opaque studies of the colon, utilizing water-soluble material in saline suspension, are helpful in further diagnosis and treatment.

Prolonged "conservative" medical treatment predisposes to phlegmonous colitis, inanition, intestinal perforation, and septicemia.

Prompt colostomy immediately proximal to the site of aganglionosis is the treatment of choice in symptomatic aganglionic megacolon in early infancy.

Colostomy done as an emergency procedure is life-saving. It affords excellent prognosis in the absence of phlegmonous colitis, inanition, intestinal perforation, or septicemia.

These patients were operated upon by members of the surgical staff of the Children's Hospital of Pittsburgh. Drs. W. B. Kiesewetter, E. S. A. King, J. J. McAleese, and T. N. Meredith permitted the inclusion of their personal cases in this review.

3500 Fifth Ave. (13).

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DISCUSSION

On Papers by Dr. Riker and Drs. Sieber and Girdany

Dr. Willis J. Potts, Chicago: These papers have presented a very interesting discussion on an extremely difficult problem—Hirschsprung's disease in the newborn. The disease presents an altogether different picture than that seen in the child who is beyond the neonatal stage.

Much of the trouble comes from delayed diagnosis and, consequently, inadequate treatment. The diagnosis is easily made if one thinks of it. When one sees a 2-, 3- or 4-day-old infant who has tremendous loops of dilated bowel with fluid levels, one thinks naturally of an atresia of the bowel. There is no objection whatsoever to performing the function of the consultant, even on a newborn baby, that is, making a rectal examination. The little finger can easily be slid into the rectum. If the infant has not passed normal, greenish, shiny-black meconium, it probably has atresia; but if it has passed greenish, shiny-black meconium, even a small amount, that child has an open bowel all the way through, and it probably has Hirschsprung's disease.

As was suggested by Riker, the finger examination will often result in an expulsion of air and a small bit of normal meconium. Then the diagnosis is made.

In the past our mortality was due primarily to prolonged medical management. One cannot treat these patients medically. They must have a colostomy above the point of aganglionosis. Once in a

while one is going to make the mistake (we have made it, and I am sure some other surgeons fall in the same category) of operating on a child with a preoperative diagnosis of atresia of the bowel. Upon opening the abdomen, no obstruction is found. In such a case the surgeon may ask one of the people who is standing by to take a fairly large catheter and slide it up the rectum, and he may, with his hand in the abdomen, direct it into the dilated portion of the bowel. If he gets normal, shiny, green-black meconium, the child does not have atresia but has Hirschsprung's disease, and nothing else. A biopsy and a colostomy then are indicated. We used to include mucosa in the biopsy specimens, but now take only the muscularis, leaving the mucosa intact. It is easily accomplished and, of course, avoids contamination. We have done such biopsies in newborn infants.

In older children Hirschsprung's disease will almost invariably give a history of constipation dating back to infancy. If a child has had constipation only in recent years, beware of a diagnosis of Hirschsprung's disease, especially if constipation came on at or about 2 years of age, when a new baby arrived in the family. The constipation is probably psychogenic and can be handled with petrolatum enemas and moral support.

Finally, in the surgery of Hirschsprung's disease the services of an experienced pathologist are essential. Even the well-trained pathologist requires much experience, in the study of hundreds of slides, before he can be certain that ganglion cells are or are not present in a microscopic section of the colon.

Dr. H. William Clatworthy Jr., Columbus, Ohio: This subject is really a very important one, and I should like to confine my remarks to confusing this audience a bit.

The importance of onset at birth and the x-ray diagnosis has been dealt with by each person who has spoken about this problem. We have had some difficulty with a particular group of newborn infants who have masqueraded as cases of true Hirschsprung's disease but who in truth actually had an obturative type of obstruction, which we now choose to call "the meconium-plug syndrome" (*Surgery* 39:131-142, 1956).

I should like to show very quickly several slides to help the audience differentiate between these two types.

(Slide) Here is a baby 2 days of age with obvious low intestinal obstruction, manifested by distention, dilated veins in the abdominal wall, and a history of vomiting bile and of having passed no stools whatever by rectum.

(Slide) The barium enema done on this infant showed a narrow left colon and a hugely distended transverse colon, and we felt that this infant probably had a long segment of aganglionic disease.

(Slide) A left transverse colostomy was performed. At 15 months of age the abdomen was reexplored and multiple biopsy specimens of the left colon were examined. The ganglion cells were found to be normal throughout.

(Slide) Therefore the colostomy was excised and a colocolostomy was performed. Three years later the child was enjoying normal bowel habit, and barium enema demonstrated a normally functioning colon.

We have now accumulated 12 such cases, the history and x-ray studies of which are quite typical. In each instance the barium enema demonstrated a small left colon with a tapered area extending into the proximal dilated colon. Frequently a radiolucent filling defect (the meconium plug) may be seen at this point.

Each of these infants was relieved of obstruction by one or two fluoroscopically controlled barium enemas and has remained completely free of obstructive symptoms.

Dr. Robert E. Berry, Ann Arbor, Mich.: I should like to compliment Dr. Riker and Dr. Sieber on their very excellent and instructive papers.

We have a small group of these cases of acute fulminating intestinal obstruction in the newborn, and I certainly should like to lend what support I can to Dr. Riker's observation that the treatment is colostomy, and that the colostomy should be placed in the transverse colon.

Two of these patients were unusually interesting. The first was an infant with acute fulminating obstruction, just as Dr. Riker demonstrated, at 4 days of age. Operation consisted of transverse colostomy. At 6 months of age the child was returned for reevaluation. A barium enema demonstrated a colon compatible with the normal picture of a colon of a child of that age. We were curious as to what would happen if the colostomy was closed. Our curiosity got the better of us, and we closed the colostomy. The answer was soon obvious. In four days a left colon obstruction developed and the colostomy had to be reopened.

A short time later a second child with the same kind of history was seen. A colostomy was done, and once more a six-month reevaluation demonstrated that the left colon seemed normal. We had some difficulty in learning our lesson, for we went ahead and closed this colostomy also, with the same result. The colostomy had to be redone at the end of three or four days because of acute mechanical obstruction.

Dr. Edwin W. Gerrish, Cleveland: I should like to congratulate the essayists on their excellent papers on a subject of great interest to me.

Unfortunately, not more than three weeks ago I finished treating what I believe is the fifth reported patient with extensive aganglionic disease. This boy clinically and roentgenologically had classical Hirschsprung's disease localized to the rectum and rectosigmoid area. A pull-through operation was done, after which his entire intestinal tract failed to function. Colostomy, tubes, and drugs failed to help. At autopsy ganglion cells were almost absent in the gastrointestinal tract, except in the esophagus, where they appeared normal.

We were able to keep him alive for nine weeks mainly through the use of intravenous fat. His death was due to a hemorrhagic episode, which we feel may have been associated with the prolonged administration of the fat.

DR. WILLIAM L. RIKER, Chicago: I think it is important at the time one does the colostomy on an infant to do also an exploratory laparotomy in the left lower quadrant. A biopsy specimen of the rectosigmoid taken at that time will prevent some worries later, because one has an absolute diagnosis made by the pathologists from the specimen that has been obtained. One does not have to worry about whether one should or should not do a resection of the colon later.

DR. WILLIAM K. SIEBER, Pittsburgh: May I thank the discussers, particularly Dr. Clatworthy for his word on differential diagnosis.

There are several other conditions that are confusing, of course; but, in line with this, one of the most helpful examinations has been the barium enema, not only for differential diagnosis but to help in determining where we put our colostomy. It is obviously very helpful to know preoperatively whether the patient will require a sigmoid colostomy or a transverse colostomy.

The argument as to whether one should do the transverse colostomy or the sigmoid colostomy, I think, is one that is a matter of the individual surgeon's preference. Our decision as to where it should be done depends upon the individual case, particularly on what has to be done later in the definitive surgical procedure.

Clinical Experience with Rigid Wire in Wound Closure

PAUL I. HOXWORTH, M.D., Ph.D., Cincinnati

Introduction

The better holding power and tolerance by tissues of stainless-steel wire [1] sutures have been attributed to the superior strength, antiseptic properties, inertness, and smooth surface without interstices.[8,11,12,15,16] Most surgeons recognize these advantages over more conventional materials, but few use the wire in the closure of abdominal fascia because of certain annoyances. It is difficult to handle in tying; knots seat poorly, and occasionally one or more sutures need to be removed because of pain produced by cut ends. The behavior of multifilament wire in infected wounds is similar to that of silk, presumably due to the interstices, in the prescence of which healing after infection is often followed by recurrence of inflammation, abscess formation, draining sinus tracts, and spontaneous extrusion or surgical removal of the suture.

A method for closure of fascia in abdominal wounds with preformed rigid wire sutures was first described three years ago.[7] Experimental studies conducted at the Cincinnati General Hospital had demonstrated flexibility of suture material to be undesirable in some respects, and rigid wire of rectangular form at the supporting ends to be superior in holding power. These studies were based on engineering principles and showed that with flexible suture material the phenomenon of "shear," * caused by the concentration of forces, is a factor in wound disruption, producing cutting and tearing through the fascia. This method also eliminated handling and tying of the wire and projection of cut ends into sensitive subcutaneous tissue.

The value of any new surgical technique is determined by prolonged trial, and preformed rigid wires have been in clinical use at the University of Cincinnati since 1953. The purpose of this paper is to describe the experience with this closure in the various clinical circumstances encountered in surgical abdominal wounds and to illustrate refinements made in the technique for placement.

Theory

The theoretical concepts and experimental studies which lead to the development of this method have been described in detail elsewhere.[7] In brief, it may be observed that flexible material exerting force against fascia takes the general form shown in Figure 1*A*, compressing the supporting edges of the fascia within the "nose" of the loop in proportion to the intensity of the forces applied. These forces become concentrated at the apex of the loop, increasing the tendency to shear or pull through. The principle of this phenomenon is that the forces are distributed unequally, and therefore less advantageously, because the radius becomes smaller and variable.

With the use of rigid wire of rectangular form, the forces are distributed over the supporting surface of the fascia more evenly (Fig. 1*B*). Under these circumstances, given the same force and with the caliber of the suture material constant, there is less tendency toward failure by cutting and tearing.

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From the Department of Surgery, University of Cincinnati College of Medicine and Cincinnati General Hospital.

* The word "shear," as used in this discussion, refers to general net cutting effect, resulting from a combination of forces in the area under stress, rather than purely theoretical, mechanical shear.

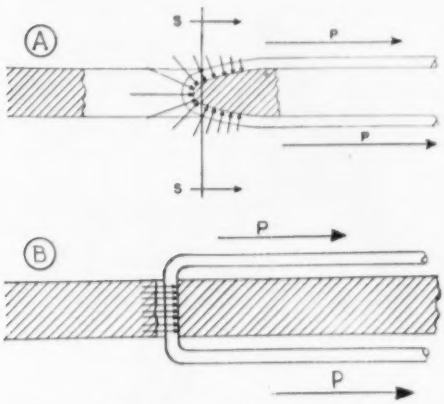


Fig. 1.—*A* and *B*, comparison of the distribution of forces in flexible suture material with rigid material of rectangular form.

Results of experiments which contrasted the effects of flexibility and rigidity upon holding power in inanimate materials and in dogs were in accordance with the above theoretical concepts, indicating the superiority of rigid wire.[7]

Technique

As with any surgical technique, it is difficult to teach the method of placement of the suture by words and printed illustration. With instruction at the operating table, the beginning user obtains satisfactory results with ease and rapidity. This has been uniformly true among the members of the resident staff at the Cincinnati General Hospital. In turn, they have made improvements in the technique which add to the simplicity of closure.

The first refinement was the development of a special carbide-tipped holding forceps with vertical jaws, which grasp the suture firmly and hold it in proper alignment without altering its shape. The best results are obtained by following the procedure illustrated in Figures 2, 3, 4, 5, and 6. The legends are designed for instruction. The common difficulty encountered in early trials is that the distal leaf of fascia is not penetrated far enough from the cut edge, and that the proximal leaf of fascia is not threaded far enough into the aperture between the prongs before it is engaged. Failure to observe these two points in the technique results in poor approximation of the fascial edges. Traction nonabsorbable (silk) or absorbable (gut) surgical sutures placed through the fascia at the extremities of the wound facilitate placement for the beginning user. Cleansing of the fascial surface by sharp dissection is helpful if the subcutaneous fat is densely adherent.

Clinical Material

A study has been made on 2535 abdominal wounds closed by this method from July, 1953, to

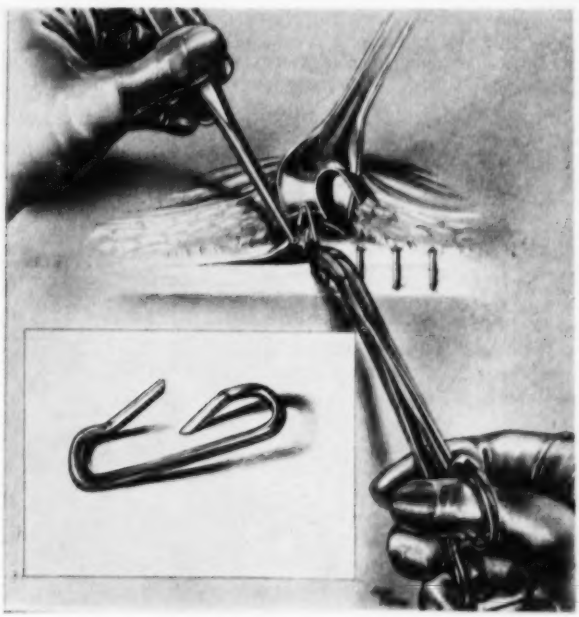


Fig. 2.—The far leaf of fascia, held with thumb forceps, is penetrated by inserting the distal prong of the suture at a point quite far from the cut edge.

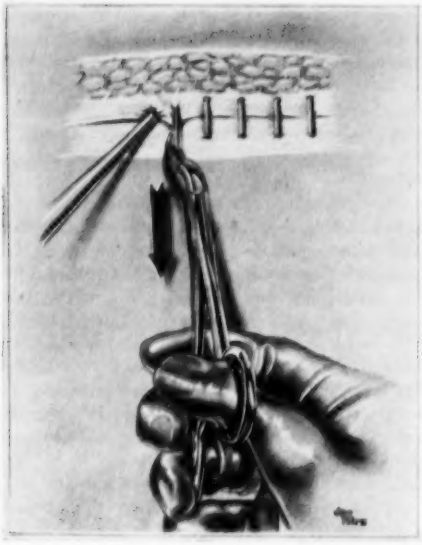


Fig. 3.—The engaged leaf is then dragged toward the operator to produce considerable temporary overlapping.

January, 1957. Transverse incisions were dealt with in about one-third of the cases, and the remainder were longitudinal. Of the closures, 1649 were by residents on service patients and 886 by attending staff members and residents on private patients. In approximately 3% of the closures, retention sutures of through-and-through

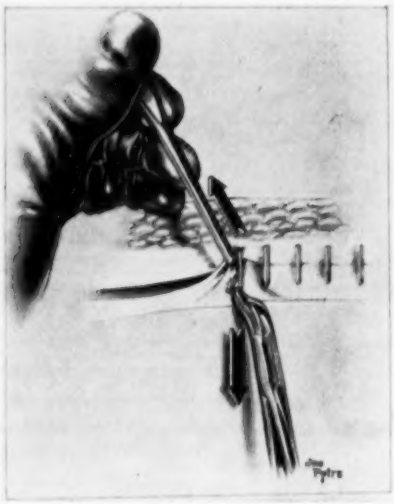


Fig. 4.—The proximal leaf is grasped and dragged upward and away from the operator, well into the aperture between the prongs.

steel wires were used in conjunction.[8] Seventy-five per cent of the patients have been followed for periods up to three and one-half years after leaving the hospital.

Observations have been made on subjects of usual clinical interest, including wound disruption and hernia, the behavior of infected wounds in the presence of the suture material, and the tolerance of the suture by the tissues and by the patients.

Results

Many factors other than suture material contribute to wound disruption, but the relationship of this complication to the new method of closure is of importance in the evaluation.[2,3,5,6,9,10,13,14] More than 30 op-

Fig. 5.—The direction of pull with the thumb forceps is then reversed and the fascia penetrated by pulling it onto the proximal prong of the suture

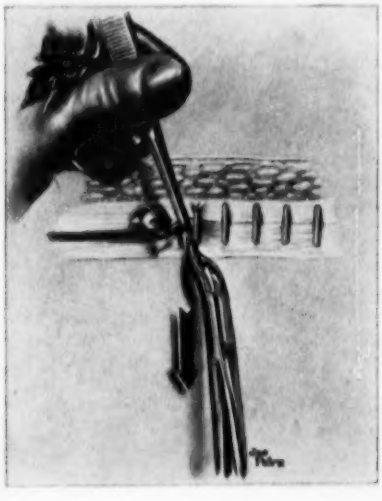
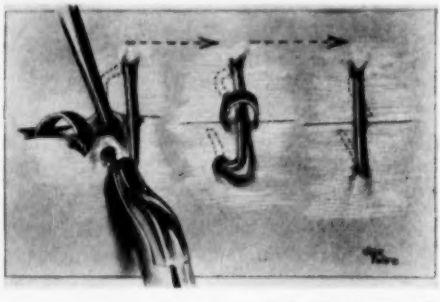


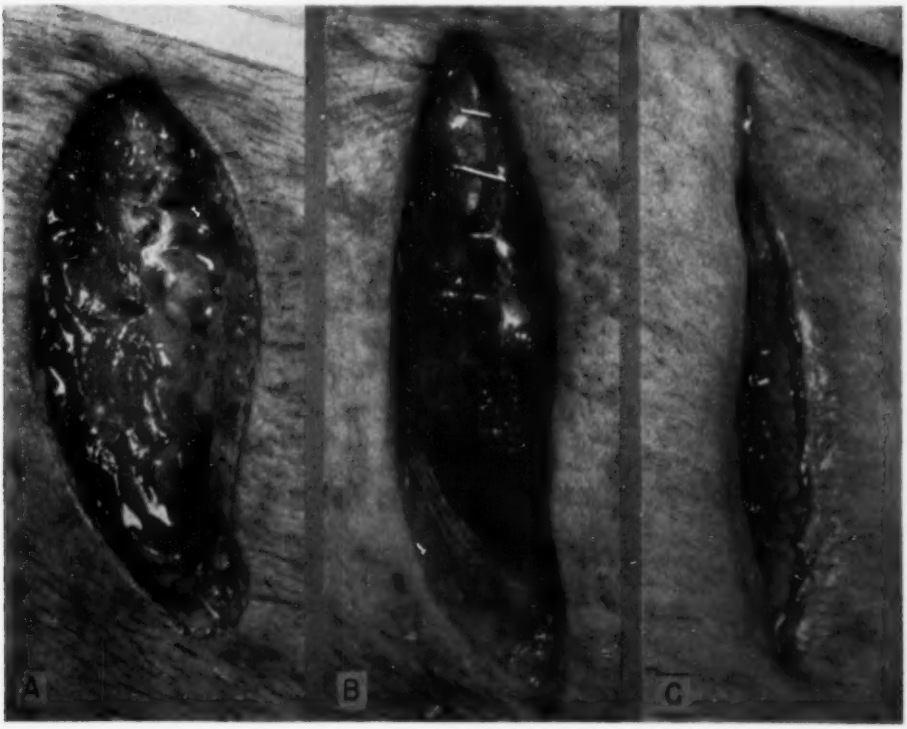
Fig. 6.—The suture is released from the holding forceps and rotates into the position of finished placement.



erators have been concerned with the 1649 closures in service patients. In this group there were seven wound disruptions. Infection, peritonitis, old age, obesity, malnutrition, and lung disease with coughing contributed. In 886 closures on private patients by 11 operators there were two wound disruptions. One occurred in the course of severe acute pancreatitis following gastrectomy for duodenal ulcer. The difference in the results of the two groups may be attributed in part to the poorer quality of the tissues often seen in free medical service patients and in part to the judgment of more experienced surgeons in using through-and-through retention sutures. In two of the patients with wound disruption it was evident at the time of secondary closure that several sutures had been engaged in dense areolar tissue anterior to, but not into, the fascia. In a third, disruption occurred between retention sutures placed much too far apart.

Infected wounds requiring drainage down to the fascia developed in 21 patients. Most of these were grossly contaminated wounds in the surgery of intestinal trauma, perforated peptic ulcer, and gangrenous bowel. Fecal fistulas developed in two additional patients, from whom sutures were removed for drainage of intra-abdominal abscesses secondary to leakage at the site of anastomosis after bowel resection. Of the 23 patients, 21 survived through the period of wound healing, including the 2 with fecal fistulas which closed spontaneously. In none of these was a suture extruded or removed during healing as the granulation tissue grew to cover the sutures (Fig. 7). In no instance has there been persistent or recurrent sinus tract formation

Fig. 7.—*A*, wound on March 29, 1955, four days after drainage of the abscess, with sutures hidden by exudate. *B*, wound on April 9, showing sutures exposed in healthy granulation tissue. *C*, wound on April 22, with healing over the sutures.



or abscesses requiring removal of a suture to promote healing.

In following this series of patients for incisional hernia, small defects in fascia may have escaped detection, and hernias may be found later. Three hernias have been detected thus far. Two followed secondary closure of wound disruptions, and one was discovered six months after surgery, with no earlier wound complication noted. All were in elderly patients with upper abdominal wounds and are small and asymptomatic. In the same four-year period at the Cincinnati General Hospital, where the suture is used routinely, 160 patients have been operated on for incisional hernia in wounds which had not been closed with the rigid wire.

While no patient has required readmission for removal of a suture because of pain or tenderness, wounds have been reopened in 32 patients for other reasons at intervals of from six days to three years. The healing of the fascia has been uniformly good, with the suture encased in a minimum of scar. All wires had retained their original rectangular form, without bending, and none were discolored, pitted or, fragmented. They are easily removed by exposing the top surface of each with sharp dissection, grasping with the holding forceps, and reversing the motions used in the placement.

Summary and Conclusions

Abdominal closure with preformed rigid wire sutures has been used in more than 2500 patients at the University of Cincinnati College of Medicine, and the results have led to its adoption as the preferred method. Wound disruption occurred in 9 patients in the series, including 2 among 886 closures made by more experienced operators. There were three incisional hernias.

Well tolerated by tissues in the presence of inflammation, subsequent healing, and latent infection, the suture need not be removed to facilitate wound healing. Spontaneous extrusion has not occurred.

Annoyances produced by the tying of annealed wire are eliminated. The suture is not handled with gloves during placement, and no patient has needed removal of a suture because of pain or tenderness.

The technical advantages of the method as compared with closure with other materials are several. The suture serves as its own needle, and the cutting of material into proper lengths, threading needles, tying knots, and material waste are obviated. The method is therefore simple and rapid, two or three minutes being ample time for unhurried placement in a large wound.

Cincinnati General Hospital.

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DISCUSSION

DR. M. M. ZINNINGER, Cincinnati: Some four or five years ago, when Dr. Hoxworth first talked to me about the use of preformed rigid clips to be used in closing abdominal incisions, I was somewhat aghast. I knew he had been trained, just as I had been, in the Halsted tradition, in which the use of soft, pliable suture materials was emphasized. However, the more I learned about the theoretical and practical aspects of his method, the more I became convinced of the validity of the physical and physiological principles involved. In my usual conservative manner, however, I waited for some time, while he and his immediate associates and the residents at the General Hospital had assembled considerable clinical data, before finally trying out the new sutures. I had heard that there was somewhat of a trick in placing them; so I asked the resident surgeon at the Cincinnati General Hospital to demonstrate the method after I had helped him with a difficult operative procedure. Placing the Hoxworth sutures did not look hard; so shortly thereafter I tried it myself. I immediately appreciated that there is a little legerdemain necessary in placing the sutures, but with proper instruction, that was quickly learned, and once learned it was possible to place the sutures rapidly and accurately. Soon thereafter I began using the method in abdominal closure in my private patients. I found that transverse and midline incisions were very suitable for the new method, but experienced trouble with paramedian incisions, in which at times one layer of the fascia is at a higher level than the other. I learned from Dr. Hoxworth that this discrepancy in level could be overcome by placing one gut or silk suture at each end of the incision, together with one or more intervening sutures if necessary. Traction on these sutures leveled off the opposing fascial layers, and the rigid sutures could then be placed without difficulty.

Over a period of months I found myself using the rigid sutures more and more frequently, until now it is the method used routinely in closing all abdominal incisions. On no occasion has there been any complication due to the sutures. I have found that they can be placed more rapidly than any other suture, that they give secure closure resistant to infection; and no patient has had complaint of pain in the incision. The resistance to infection is phenomenal. At the time when I was just beginning to use these sutures I had occasion to observe their behavior in infected wounds at the Cincinnati General Hospital. Here, I saw on ward rounds an infected wound. The skin and subcutaneous tissues were open, and the fascia with the rigid wire sutures was exposed. Under ordinary circumstances the sutures might have been removed, but these were not. As the infection cleared up and granulation tissue appeared, the sutures were engulfed and covered. The wound healed completely without sinus formation. Evidently bacteria find no foothold in this suture material.

On several occasions I have found it necessary to reenter the abdomen through an incision previously closed by this method. This has occasioned no particular difficulty. Several knife blades may be dulled; but once the sutures are exposed, they are found to be surrounded by minimal reaction and can be "backed out" by grasping them with a clamp and reversing the manipulations used in placing them. Furthermore, they exert no hazard when it is necessary to give postoperative radiation therapy to abdominal tissues in which they have been used to close the wound.

Those of you who attended the clinical day preceding the meeting of the Western Surgical Association in Cincinnati last November will recall that all the abdominal incisions made that day were closed with these sutures. No instructions were given the residents to use this method of closure, and that it was used in all cases only emphasized the fact that it is preferred to other methods of closure.

I believe that Dr. Hoxworth is to be complimented on the development of a new method of abdominal wall closure which has been demonstrated to be superior in many respects to methods used in the past. I would heartily recommend to all of you that you use it, because I am sure that you will find it valuable, just as I and many others have already found it.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: How many in the audience have used this suture? About five of you. I had not appreciated the fact that you had had eviscerations. I looked up my own experience with wound complications and found we had so many eviscerations that we were hesitant to say anything about them. Apparently, eviscerations occur regardless of the type of suture material used. I should like to ask Dr. Hoxworth his explanation for the majority of eviscerations.

DR. PAUL I. HOXWORTH, Cincinnati: In answer to Dr. Zollinger's question on how to prevent wound disruption, it would be redundant to express views concerning wound disruption in an instructive way to this group, except to say that there is no panacea. No layered closure can ever substitute for the use of retention sutures when indicated in the judgment of the operating surgeon.

In the only publication made on this method, the original one in *Annals of Surgery*, I emphasized that it was not to be employed or thought of as a substitute for through-and-through steel- or silver-wire closure when indicated.

Coma with Increased Amino Acids of Brain and Cerebrospinal Fluid in Dogs with Eck's Fistula

Prevention By Portal-Systemic Collateral Circulation

JESSE L. BOLLMAN, M.D.; EUNICE V. FLOCK, Ph.D.; JOHN H. GRINDLAY, M.D.; REGINALD G. BICKFORD, M.B., and FRANK R. LICHTENHELD, M.D., Rochester, Minn.

Portacaval anastomosis with diversion of all the portal blood from the liver (Eck's fistula) in dogs is followed by characteristic symptoms and death within a year. A similar surgical procedure performed on humans for the relief of bleeding esophageal varices does not produce similar symptoms. In this study we show that symptoms do not follow this operation in the dog if portal-systemic collateral circulation is present. Since the presence of excessive portal-systemic collateral circulation is one of the chief indications for this operation in man, the absence of symptoms similar to those of animals with Eck's fistula also may be related to this collateral circulation.

The course and symptoms in animals with Eck's fistula were described adequately more than 60 years ago by Hahn and associates.[1] In our experience, the same symptoms have prevailed. If all the portal blood is diverted from the liver to the vena cava in the absence of changes in collateral circulation, the animal loses weight almost progressively and dies within a year after operation. In the relatively few of our dogs which have not lost considerable weight after operation, exploration or portograms have shown that the portacaval fistula was closed, or an accessory vein was carrying portal blood to the liver, or some portal blood was diverted to the systemic veins by collateral vessels. The animal usually becomes stuporous in less than three months and passes into the characteristic coma. The coma may deepen and the animal may die within a day or so, or improvement may occur. The animal may regain some of its lost weight, but never to the extent of complete recovery. Within a week or so coma usually recurs. Improvement again may take place and subsequent episodes of coma later occur. As many as 10 such episodes have been noted within three months, before terminal coma has appeared. We have been unable to determine any prognostic index that is of value in suggesting which attack will be terminal.

Results of our attempts to alter the course in animals with Eck's fistula by dietary means have not been consistent. Statistical evaluation of the effects of inclusion of large amounts of nitrogenous material in the diet (meat, amino acids, urea, ammonium salts) indicated a shorter average survival time in such animals than in similar animals fed diets containing none or small amounts of these substances. The difference, however, was small, and long or short survivals occurred in each series. We have been unsuccessful in finding a consistent treatment for coma. Spontaneous recovery often occurs, and we also apparently have relieved coma by many therapeutic measures, such as the administration

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Section of Biochemistry (Drs. Bollman and Flock); Section of Surgical Research (Dr. Grindlay); Section of Physiology (Mr. Bickford), Mayo Clinic and Mayo Foundation. Fellow in Surgery, Mayo Foundation (Dr. Lichtenheld). The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

of antibiotics, glutamic acid, glutathione, and methionine, intravenous injection of dextrose with or without vitamin supplements, and use of enemas. Each method also has failed to alter the coma in animals which could not be distinguished from comatose dogs in which treatment apparently was effective.

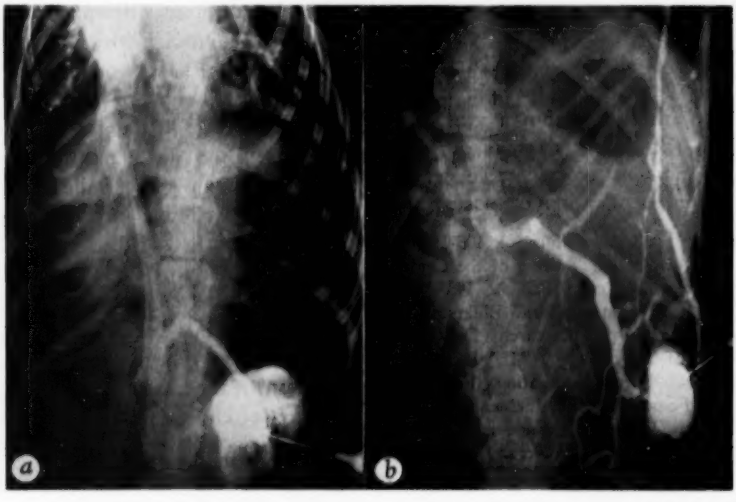
The coma of animals with Eck's fistula resembles in many respects that occurring terminally in animals after complete removal of the liver and subsequent maintenance by administration of dextrose. Except for the fact that improvement may occur spontaneously, with or without treatment, in the coma associated with Eck's fistula, careful observation has not shown any characteristic differences in the nature of the coma. Chemical changes in the blood, urine, cerebrospinal fluid, and brain also appeared to be similar after hepatectomy and during the coma caused by Eck's fistula.

Present Study

Every one of our animals with Eck's fistula which has shown an open portacaval shunt with no blood entering the liver by the portal vein and an absence of portal-systemic collateral circulation had typical symptoms and died within a year after operation (Fig. 1*a*). Thus, in a recent series of 22 dogs, the first animal died at four weeks and the others died subsequently at irregular intervals until all were dead after nine months. In other series, we have observed dogs which maintained their weight and showed no symptoms after the Eck fistula was established. In each of these animals it was found that the portacaval shunt was closed, that portal collateral vessels had bridged the ligature of the portal vein and portal blood was reaching the liver, or that collateral portal-systemic circulation had developed.

Collateral Circulation.—The presence of collateral circulation alters the course of animals with Eck's fistula.[3] Portacaval

Fig. 1.—Percutaneous splenoportograms[2] of dogs with Eck's fistula. (*a*) Note absence of collateral circulation from portal vein and absence of portal circulation to liver. This animal had severe symptoms and died four months after operation. (*b*) Note absence of portal circulation to liver. The collateral circulation that is evident was developed by serial complete occlusion of the portal vein at its entrance to the liver six weeks prior to the establishment of Eck's fistula. This animal was in excellent condition six months after the operation, when this splenoportogram was made. At that time, gradual occlusion of the vena cava just below the portacaval anastomosis was begun. Symptoms typical of those associated with Eck's fistula developed rapidly, and the animal died four months later.



shunt with occlusion of the vena cava above the anastomosis so that caval blood is diverted into the portal vein results in pronounced portal-systemic collateral circulation; therefore subsequent occlusion of the portal vein at its entrance to the liver may be accomplished without the production of symptoms. Such animals subsequently gain weight and do not exhibit the symptoms associated with ordinary Eck's fistula. In the present study, we have garnered valuable information by producing similar anatomic changes, but in a different sequence. Portacaval anastomosis with complete ligation of the portal vein was followed by typical symptoms and coma. When coma had appeared, partial occlusion (about two-thirds) of the vena cava above the portacaval anastomosis was attempted. Except for the dogs dying immediately, all the animals recovered, gained back their normal weight, and showed no further symptoms. On the other hand, partial occlusion of the vena cava below the portacaval anastomosis with ligation of the portal vein produced symptoms typical of those occurring with Eck's fistula, but they appeared more rapidly than in uncomplicated Eck's fistula.

To study further the effects of collateral circulation in dogs with Eck's fistula, we made the following studies. The portal vein in 10 dogs was partially occluded by a linen ligature; it was occluded further 10 days later, and after another 10 days it was completely occluded at its entrance to the liver, at which time the spleen was transplanted under the rectus muscle. Splenoportography after six weeks revealed a considerable degree of portal-systemic collateral circulation and the absence of portal flow to the liver (Fig. 1*b*). Portacaval anastomosis then was done. Each of the 10 dogs survived, gained weight, and appeared normal. Six months later all were in excellent condition, being greatly different from dogs with uncomplicated Eck's fistula. Splenoportography at that time revealed that collateral circulation was still present; the portacaval anastomosis was open, and none of the media injected into the spleen entered the liver. The vena cava then was occluded almost completely just below the portacaval anastomosis in each dog. All the animals recovered from the immediate effects of this operation but lost weight, had symptoms typical of those produced by Eck's fistula, and died within three months. Certainly, the course and symptoms of animals with Eck's fistula depend on some factor in addition to the portacaval shunt and diversion of portal blood from the liver.

Cerebrospinal Fluid and Brain.—Study of samples of cerebrospinal fluid withdrawn from 20 dogs during coma resulting from Eck's fistula showed that the total content of free amino acids was normal or slightly increased in 7, about twice normal in 7, three times normal in 3, and four times normal in 3 (Fig. 2). In every case the increase was mostly in glutamine. Two-dimensional paper chromatography, with phenol-cresol as the solvent in one direction and 2, 4-lutidine as the solvent in the other direction, was employed to separate the free amino acids. After spraying with triketohydrindene hydrate (ninhydrin), the isolated spots were eluted and compared spectrophotometrically at a wavelength of 570mμ, with known amounts of each amino acid treated in the same manner. Phenylalanine, leucine, valine, tyrosine, alanine, threonine, glutamine, aminoacetic acid (glycine), serine, glutamic acid, aspartic acid, and histidine could be well quantitated in this way. None of these amino acids were in quantities less than those of normal animals, and each was found to be increased to some degree when the total content of free amino acids of the cerebrospinal fluid was increased. No single amino acid was predominantly increased except glutamine, as already noted. There was no correlation with the length of the postoperative periods in the dogs with Eck's fistula or with the degree of loss of weight. No correlation was present with the duration or intensity of the coma just prior to withdrawal of the cerebrospinal fluid. There did appear to be

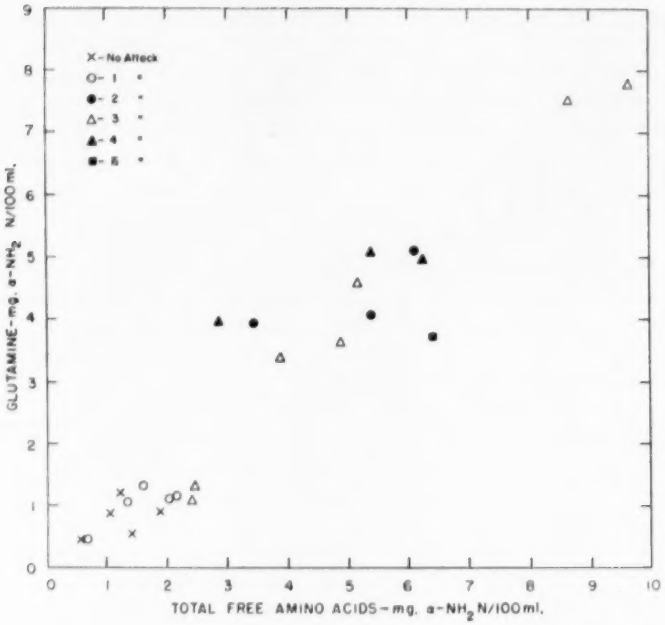


Fig. 2.—Concentration of total free amino acids and glutamine, expressed as milligrams of alpha-amino nitrogen per 100 ml., in the cerebrospinal fluid of dogs with Eck's fistula.

a tendency toward greater values for glutamine and amino acids with subsequent attacks, but this increase was not progressive. Between attacks, the content of amino acids in the cerebrospinal fluid reverted toward normal.

We secured the brains of 14 animals with Eck's fistula when death in coma appeared imminent. In each of these, the cerebral content of free amino acids apparently paralleled that of the cerebrospinal fluid (Fig. 3). The quantity of free amino acids in the brains of normal animals is about 10 times that of cerebrospinal fluid, and approximately the same ratio was maintained in the dogs with Eck's fistula; as in the cerebrospinal fluid, the content of glutamine was increased most. Some of the animals in coma had normal concentrations of free amino acids in the brain. The relationships of the free amino acids of the brain to the coma and to the condition of the dogs with Eck's fistula were similar to those of the free amino acids of the cerebrospinal fluid.

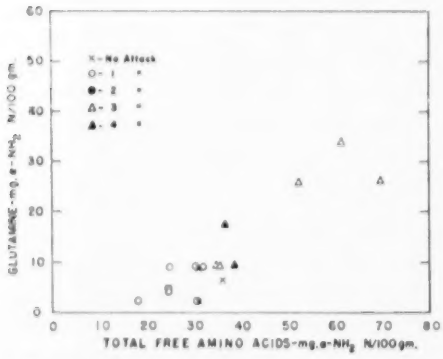


Fig. 3.—Concentration of total free amino acids and glutamine, expressed as milligrams of alpha-amino nitrogen per 100 gm. of tissue, in the brains of dogs with Eck's fistula.

At no time were we able to demonstrate any appreciable increase in the amount of free amino acids in the plasma of dogs with Eck's fistula, even in those which had large increases in free amino acids of the brain and cerebrospinal fluid. This lack of parallelism also occurs after hepatectomy in dogs which receive dextrose and insulin.[4-6] Pronounced increases occur in the free amino acids of the brain, cerebrospinal fluid, blood, and muscle after complete re-

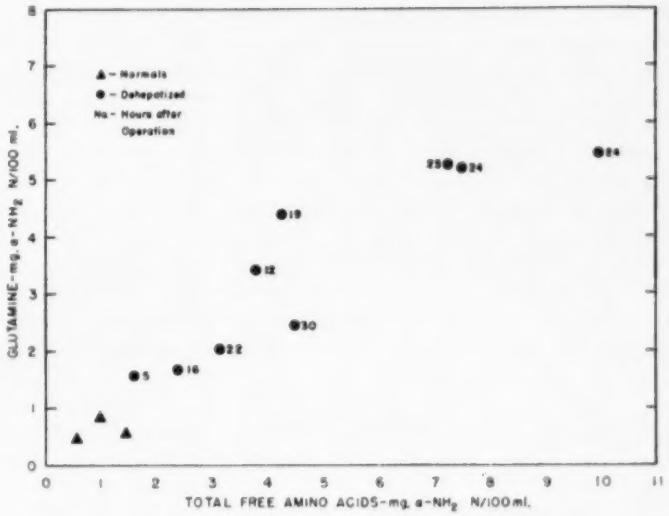


Fig. 4.—Concentration of total free amino acids and glutamine in the cerebrospinal fluid of dehepatized and normal dogs.

moval of the liver (Fig. 4); however, administration of dextrose in the presence of insulin reduces the content of amino acids in the blood and muscles without altering the increase in the brain. The increase of free amino acids in the brain and cerebrospinal fluid that occurs after hepatectomy is progressive; the terminal coma of these animals is characteristic but cannot be correlated with the degree of increase in any of the free amino acids that we have measured in the brain or cerebrospinal fluid.

Electroencephalography.—Electroencephalographic studies showed a definite difference between the coma of animals with Eck's fistula and the coma of hepatectomized animals. We were unable to obtain satisfactory electroencephalographic recordings with cutaneous electrodes on animals because of interference from the muscles. Satisfactory recordings were obtained by the use of fine wire electrodes implanted directly on the dura through small holes bored in the skull. The insulated electrode wires were embedded in Acrolite (a synthetic plastic), which was molded to fit the defect in the skull. The wound was closed around the Acrolite plug, which healed in place, and connections from the plug gave

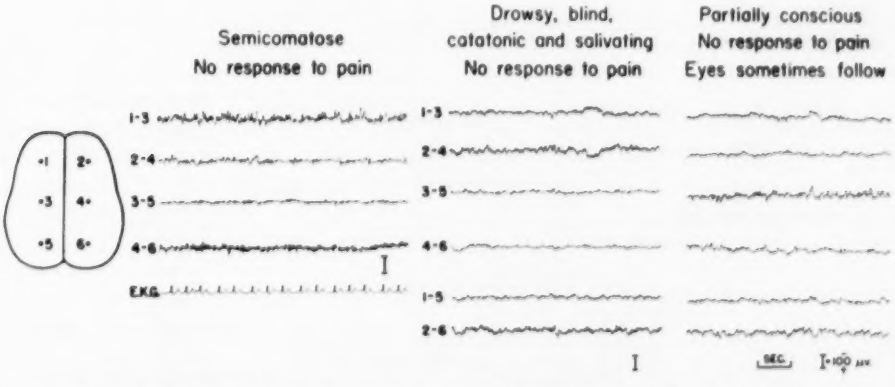


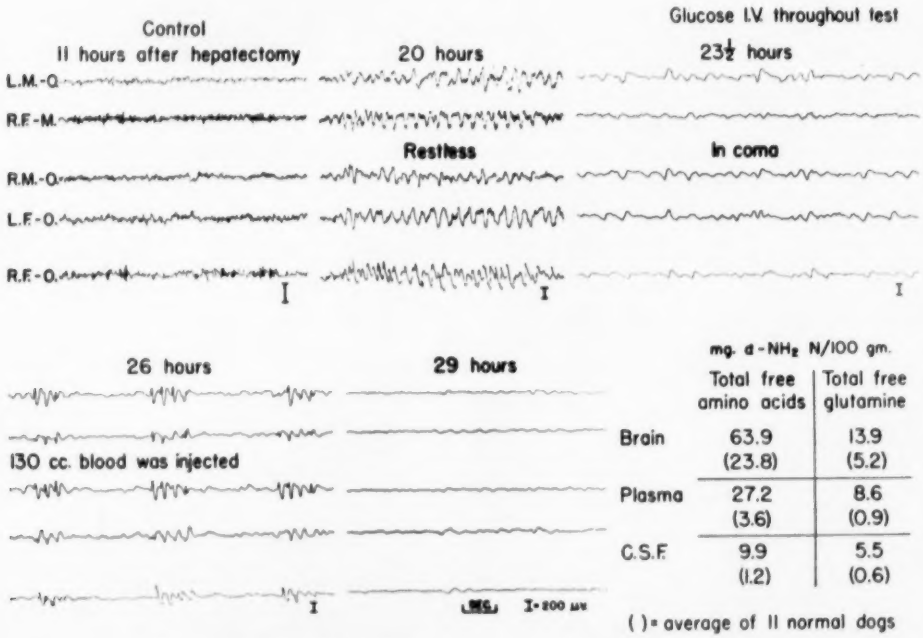
Fig. 5.—Minimal electroencephalographic changes in comatose dogs with Eck's fistula.

satisfactory recordings as long as six months after operation.

We obtained 40 electroencephalographic recordings on 16 dogs with Eck's fistula which were in coma after the usual typical symptoms. None of these records showed any significant deviations from previous records on the same animal, and all patterns were essentially normal (Fig. 5). In the extremely late lethal phase of the attacks associated with Eck's fistula, we were able to demonstrate electroencephalographic changes that had a "seizure" pattern. This was combined with repetitive sharp-wave-like discharges. All the animals showed flattening of the electroencephalographic waves coincident with terminal cardiac failure.

For comparison, satisfactory electroencephalographic recordings were obtained during coma after complete removal of the liver on 4 dogs, 4 cats, and 11 rats. These were definitely different from the recordings obtained on the dogs with Eck's fistula. Up to 18 hours after operation, the electroencephalograms of these dehepatized animals showed occasional bursts of activity with a frequency of 4 to 5 waves per second, with a normal background record. Later, when these animals were in coma, the frequency decreased to 2 or 3 each second, and triphasic waves appeared resembling those seen in hepatic coma in humans.[7] The triphasic waves occurred more frequently in groups with ensuing time. Finally, the waves began to flatten and activity disappeared. Up to this time no change was noted in the electrocardiogram or in respiration. Death usually occurred about 15 minutes after the waves became flattened. Prior to coma the hepatectomized animals appeared hyperexcitable and showed an augmented electric response to stimuli. Later, when the animals were comatose, responses could not be elicited. These changes are evident in Figure 6.

Electroencephalograms were obtained from dogs which were receiving continuous injection of ammonia in doses of 150 mg.



	mg. d-NH_2 N/100 gm. Total free amino acids	Total free glutamine
Brain	63.9 (23.8)	13.9 (5.2)
Plasma	27.2 (3.6)	8.6 (0.9)
C.S.F.	9.9 (1.2)	5.5 (0.6)

( ) = average of 11 normal dogs

Fig. 6.—Electroencephalographic records from a dog after hepatectomy.

of NH_3, buffered with sodium bicarbonate, per hour per kilogram of body weight. These animals showed progressive stages of restlessness, nausea, vomiting, twitching of muscles, semicoma, coma, and death; these symptoms are similar to those seen in animals with Eck's fistula.[8,9] The animals with Eck's fistula died after one or two hours of injection of ammonia at this rate, whereas normal animals survived for six or more hours of such continuous injection, and animals with extensive portal-systemic collateral circulation, developed after gradual occlusion of the portal vein, survived for periods intermediate to these extremes. Similar symptoms, apart from the time of occurrence, appeared in each of the animals. Most of the electroencephalographic abnormalities occurred in association with electrocardiographic changes, respiratory irregularities, or convulsions; during periods of coma free of these irregularities, electroencephalograms indicated much diffuse slow activity, but no waves characteristic of hepatic coma. The typical electroencephalogram in coma induced by intoxication with ammonia appears to differ from that seen in coma of liverless animals and also from the essentially normal recordings found in the coma of animals with Eck's fistula.

Summary

Portacaval anastomosis that diverts all the portal blood from the liver into the vena cava at the site of the anastomosis is followed by a characteristic sequence of symptoms. Great loss of weight, anorexia, stupor, episodes of coma, and death ensue in less than a year. The occurrence and course of these symptoms are not altered greatly by dietary changes. If additional portal-systemic collateral circulation is present, the animals with Eck's fistula do not have symptoms and they survive indefinitely.

The coma of animals with Eck's fistula is similar in many ways to that which follows complete removal of the liver. In both instances there may be pronounced increase in the amount of free amino acids of the brain and cerebrospinal fluid; glutamine is increased predominantly. The duration or intensity of the coma is not correlated with the increases observed in the free amino acids. Electroencephalographic records taken during coma after hepatectomy indicate a slowing of the brain waves and the appearance of triphasic waves resembling those seen during hepatic coma in humans. During the coma of animals with Eck's fistula, the brain waves appear normal, with the occasional appearance of a "seizure" pattern. The typical electroencephalogram during coma induced by intoxication with ammonia appears to differ from that seen in the coma associated with Eck's fistula or the coma of hepatic deficiency.

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DISCUSSION

DR. LESTER R. DRAGSTEDT, Chicago: I had an opportunity to read this remarkable contribution by Drs. Bollman and his associations *in extenso*, and I must say that I am very much impressed with this study.

I had previously been quite satisfied with the explanation that meat intoxication in Eck-fistula dogs can be accounted for on the basis of a failure in the detoxicating function of the liver. The blood from the intestine does not go through the liver, and consequently materials in that blood are not detoxified. This clear-cut demonstration makes that interpretation invalid, it seems to me.

I have made a number of Eck-fistula animals in my lifetime, and I cannot recall that I was ever impressed with any striking changes in the condition of the intestine; but I must confess that my observations were superficial. I am wondering whether the present authors have observed any long-standing pathological changes in the intestine of Eck-fistula animals that have not been described heretofore.

Their observation that the presence of collateral circulation prevents the meat intoxication syndrome suggests that it must be due not to failure of the detoxicating function of the liver but, rather, to some impairment in the detoxicating function of the intestinal tract, or possibly that the intestinal tract no longer exerts its property of selective absorption. I wonder whether the authors have made some observations on this point.

Years ago, when Dr. Bollman called attention to the fact that the substitution of a meat diet by a carbohydrate diet in Eck-fistula dogs prevented this syndrome of meat intoxication, I wondered whether the bacteria in the intestinal tract played any role in this disease. I suspect, in view of the tremendous number of experiments these authors have done, that they probably have given antibiotics of one type or another to these animals to see whether sterilization of the intestine has any effect on the production of toxic substances in the intestine which might play a role in this disease.

This paper is a very interesting scientific contribution, and one that is now very practical because of the prevalence of portacaval shunts in clinical practice.

DR. BERNARD FISHER, Pittsburgh: I, too, would like to congratulate Dr. Bollman and his colleagues on this study. We have been interested in this problem in our laboratory for several years. It has been of interest to us to find that following portacaval shunt, as originally described in 1877, there have been published no really concerted studies on portal pressures following the Eck fistula in animals.

In a paper to be published shortly, we have found that following shunting in the normal animal one does not get a drop in portal pressure; in fact, in a high incidence of animals the portal pressure increases after the ordinary end-to-side shunt.

We have been investigating the portal pressure changes following Eck fistula, that is, the increase in pressure, with the possibility that this may be what is leading to some of the problems Dr. Dragstedt mentioned, namely, faulty absorption and other disturbances of the intestinal tract.

DR. J. L. BOLLMAN, Rochester, Minn.: Dr. Dragstedt in a very short time brought up a number of points. We have had some experience in connection with most of them. Unfortunately, we haven't any answers; we have just experience.

I can say that one of the things that shows up in reference to intestinal function almost invariably, certainly in 90% of the animals that begin to go into coma following Eck fistula, is an initial period of constipation. There have been regular daily movements for a period of time, and then there is no movement for perhaps a week. Subsequently, or about that time, the animal will go into coma. We used enemas and have had some remarkable cures with just an enema. We have also had some remarkable failures with enemas.

We have used antibiotics. In order that antibiotics be effective, we wash out the intestine first. Most antibiotics are not very effective with the intestine full. Certainly we have seen no particular change after the use of antibiotics. It may be that there is some organism that we are not touching with the antibiotics that we have used. We have reduced the level of blood ammonia with enemas and antibiotics without any change in the condition of the animal. The gross and microscopic examinations of the intestine have been entirely normal in appearance as far as we can tell.

There is one study that we have not done, and that I think we should do; that is, to determine the amount of lymph flow from the intestine in the Eck-fistula animal. We have not done that; maybe that will give us some information.

Concerning Dr. Fisher's comment on the portal pressures, our findings have been that they are essentially normal. The portal pressure in the dog is quite low, and the variations up or down that we do find are minor. We find about the same range in our normal animals, and I do not see that we can ascribe anything particularly to portal pressure. The first slide mentioned lower and the higher pressures, but actual measurements indicate only slight and variable pressure changes.

Plastic Grafts for Aortic Substitution in Man

HARRIS B. SHUMACKER Jr., M.D., Indianapolis

A steadily increasing need for blood vessel substitutes has arisen as a result of recent advances in the treatment of aneurysms, coarctation of the aorta, and obstructive lesions of the aorta and major arteries. Autogenous veins may be used for peripheral arterial grafts but are not suitable for aortic replacement. Preserved homologous arteries have, in general, served well. They are, however, difficult to procure in adequate numbers. They have the additional theortical disadvantages of not surviving as living structures and of being subject to late degenerative changes. In at least a few instances, they have been followed by aneurysmal dilatation or disruption. It has, therefore, seemed logical to inquire into the possibility of using inert plastic grafts. Voorhees, Jaretzki, and Blakemore[1] were the first to demonstrate that tubes of Vinyon N cloth could be employed successfully for grafts to the canine aorta. Shortly afterward my associates and I began to study a number of plastic fabrics and to compare them with freeze-dried homologous grafts.[2-5] The results of these studies were encouraging, and we have employed plastic grafts clinically for over three and one-half years.

This report concerns our clinical experience with the use of plastic grafts for aortic substitution and for grafts between the aorta and its tributaries. A few of these cases have been previously reported.[6-10]

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Clinical Material

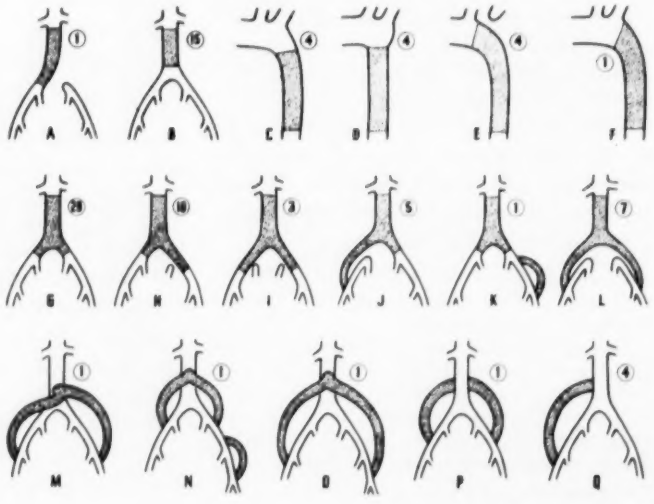
Ninety-two such cases form the basis for this study (Table). There were 61 cases of aneurysm of the abdominal aorta, 8 cases of aneurysm of the thoracic aorta, 5 cases of coarctation of the aorta, 12 instances of arteriosclerotic occlusive disease, and 6 miscellaneous cases. The hospital mortality was respectably low in certain categories and disappointingly high in others. There were 37 cases of unruptured abdominal aortic aneurysm not complicated by previous myocardial infarction. Two of these patients died in the hospital—one of rupture of an untreated thoracic aortic aneurysm on the 3d postoperative day, another of a massive pulmonary embolism 13 days after operation. There were 12 cases of arteriosclerotic occlusive disease. Unfortunately, one of these patients died of aspiration pneumonitis two days after operation. Of five cases of coarctation of the aorta, one, regrettably, died on the seventh day, of secondary hemorrhage from a large collateral artery in the chest wall. The mortality was higher in the other groups. Of 13 patients with ruptured aortic aneurysms, 7 died. Ages in the fatal cases were 54, 63, 69, 70, 76, 80, and 82, respectively. One died of cardiac arrest at the completion of the operation; one, of gangrene of the descending colon; one, of uncontrolled hemorrhage from the retroperitoneal tissues into which the extravasation had occurred, one, of atelectasis following repair of a wound evisceration, and three, of lower nephron nephrosis, 10 to 16 days after operation. Of 11 patients with an abdominal aortic aneurysm and previous myocardial infarction, 5 died in the hospital. One developed cardiac arrest during the operative procedure and, in spite of

Cases in Which Plastic Grafts Were Used for Aortic Substitution

Diagnosis	Age, Yr.		No. of Cases	Hospital Mortality
	Range	Average		
Abdominal aortic aneurysm, not ruptured or complicated by previous myocardial infarction	32-83	64.5	37	2 (5%)
Ruptured abdominal aortic aneurysm	54-82	68	13	7 (54%)
Abdominal aortic aneurysm with previous myocardial infarction	61-72	66	11	5 (45%)
Arteriosclerotic occlusive disease	38-58	53	12	1 (8%)
Coarctation of aorta	12-32	22	5	1 (20%)
Thoracic aortic aneurysm	34-76	58	8	6 (75%)
Miscellaneous	57-78	67	6	4 (67%)

resuscitation, succumbed later that night. Three died of fresh myocardial infarction, and the probable cause of death was the same in the other case. The mortality was very high in patients with a thoracic aortic aneurysm, only two of eight surviving. The causes of death included ventricular fibrillation, extensive atelectasis, and postoperative bleeding from the adherent lung or chest wall or from a transfusion reaction. In the miscellaneous group were several relatively hopeless cases. One was that of a 73-year-old man with a recently thrombosed aortic-iliac aneurysm with irreparable thrombosis of the entire distal arterial tree; another, a patient with a ruptured iliac aneurysm, in profound shock, oliguric, and with a hemoglobin of 3.3 gm. per 100 ml.; another, an oliguric patient who ruptured the aorta proximal to the line of anastomosis with the graft one month after resection of an aortic aneurysm. The fourth patient died of a transfusion reaction after operative treatment for bilateral iliac aneurysm. Only two of the six patients in this group survived.

Following the patients' discharge from the hospital, several deaths occurred. One patient died four months after excision of a ruptured abdominal aortic aneurysm of perforation of the aorta proximal to the graft at the point at which the aorta had been cross-clamped. A second patient who had a similar difficulty a month after operative resection of an aneurysm has just been mentioned. Another died of a second coronary occlusion six weeks after removal of an abdominal aortic aneurysm, while still another, an 82-year-old man, died of heart failure 25 months after successful extirpation of an abdominal aortic aneurysm. Another patient died of a basal skull fracture several months after she returned home following successful treatment for aortic-iliac and femoral occlusive disease. The others are alive and well.



Diagrammatic representation of sites of grafts.

Grafting Procedures

In the Figure are diagrammed the sites of the grafts inserted. In the first case, that of a patient in profound shock from rupture of an abdominal aortic aneurysm, no graft of suitable size was available at the time of operation, and a straight graft was interpolated between the aorta and one iliac artery, the other thrombosed iliac artery being simply ligated. In 15 cases a straight abdominal aortic graft was used, and in four others, a straight thoracic aortic graft. In four instances a graft was inserted between the base of the subclavian artery and the descending thoracic aorta. In five instances a curved graft was interpolated between the arch of the aorta and the descending thoracic aorta. In 29 cases a Y-graft was sutured to the aorta, above, and both common iliac arteries, below. In 10 cases the graft extended from the aorta to one common iliac and to one external iliac artery. In three cases the graft was interpolated between the aorta and both external iliac arteries. In five instances the graft was fixed to the aorta, above, and to one common iliac and one femoral artery below. In one case an aortic-bilateral common iliac graft was used, and another, a by-pass, graft was placed between the external iliac and the superficial femoral arteries on one side. In seven instances the graft was sutured to the aorta end-to-end and end-to-side to both femoral arteries. In one patient a graft was interpolated end-to-side between the aorta, above, and both femoral arteries, below. In another the graft was sutured end-to-side to the aorta, above, and to both external iliac arteries, below, and an additional, a by-pass, graft was placed on one side between the femoral and the popliteal artery. In another case it was necessary to place a graft end-to-side between the aorta, above, and one femoral and one popliteal artery, below. In one patient two grafts were interpolated end-to-side between the aorta and both external iliac arteries. In four instances the graft was sutured end-to-side to the aorta, above, and one femoral artery, below.

Plastic Aortic Grafts

Nylon-Polyethylene (Polythene)-Nylon.

Our first experimental study was concerned with the use of a very thin nylon cloth* which had been found satisfactory for the closure of experimentally produced cardiac septal defects. This particular fabric had great porosity, and initially a considerable loss of blood occurred through it. We, therefore rendered it impervious by heat fusion of a thin layer of polyethylene (Polythene)† between two layers of the cloth. Such grafts were employed for aortic or aortic bifurcation replacement in 13 clinical cases. In one patient a late death may have been related to the graft itself. This case will be mentioned later in some detail. The other grafts functioned well. One graft examined at exploratory laparotomy 22 months after insertion was found to be in good condition, without dilatation or other abnormality. Another, inserted after removal of an abdominal aortic aneurysm in an 80-year-old patient with chronic heart failure, was studied after death from heart failure 25 months after operation. It was in excellent condition and showed neither encroachment upon the lumen nor dilatation.

Methyl Methacrylate-Coated Nylon.—During our initial experimental studies, investigations were also carried out upon the same thin nylon fabric coated with a film of methyl methacrylate. One such graft was used in April, 1954, in the case of a 75-year-old man with a large abdominal aortic aneurysm to bridge a defect from the aorta just below the renal arteries to both common iliac arteries. It has functioned well, and the patient has remained in good health.

Nylon Filter Fabric.—As more experience was obtained in the experimental laboratory, it became obvious that grafts

* 24 F nylon fabric. The Stehli Company, Inc., 1372 Broadway, New York.

† PE-2600 Polythene film, 0.0015 in. thickness. Clay-Adams Company, Inc., 308 Washington St., Chicago.

made of nylon filter fabric‡ and the braided nylon tubular grafts of Edwards and Tapp [11]§ were superior to the grafts made of fused nylon and polyethylene and to methyl-methacrylate-coated nylon grafts. Indeed, they gave near-perfect results and forced us to conclude that experimentally they were probably even better than homografts, in view of the fact that they did not show any late degenerative changes, such as were evident in some of the homografts. Such grafts were employed in 58 clinical cases. They worked well in all of them.

Nylon Filter Fabric and Braided Tubular Grafts.—In six additional cases, braided nylon tubular grafts were sutured to one or both iliac extensions of a Y-shaped filter fabric graft when it was necessary to insert one or both distal ends of the graft into the femoral artery. These grafts worked well in five cases. In one case, the femoral extension of the graft became occluded on the seventh postoperative day during a period of shock associated with wound disruption. Though this combination of a filter fabric Y-shaped graft and one or more more braided nylon tubular graft extensions functioned satisfactorily, I prefer to use instead bifurcation tubular grafts, now that they are available, whenever a graft must be interpolated between the aorta and the femoral arteries.

Braided Nylon Tubular Grafts.—Braided nylon tubular grafts were used in 14 patients. In four patients a straight crimped graft was interpolated between the aorta and one femoral artery. In another, two such grafts were used between the aorta and both external iliac arteries. In eight cases bifurcation grafts were placed either end-to-end or end-to-side to the aorta, above, and end-to-side to the femoral or popliteal arteries, below. In another patient such a graft was interpolated between the aorta and both external iliac arteries, and a straight graft was used to bridge a femoral-popliteal obstruction. In general, these grafts proved satisfactory.

Use and Fate of Plastic Aortic Grafts

In 92 cases the use of plastic grafts for substitution of the aorta has shown itself to be altogether gratifying. The plastic grafts are a little more difficult to suture to the host vessel than are homografts, but this presents no real problem. The nylon filter fabric grafts and the grafts made by heat fusion of polyethylene and nylon fabric or nylon fabric grafts coated with methyl methacrylate were generally sutured to the artery with an everting mattress suture. In most instances the everted edges were caught with a simple over-and-over suture after placement of each mattress stitch, according to a modification of the Dorrance technique. The anastomoses of the braided nylon tubular grafts were accomplished with a simple over-and-over suture. No cuff was turned back. The filter fabric grafts were cut on the bias, and the ends did not tend to fray. The nylon fabric fused with polyethylene or coated with methyl methacrylate, similarly, did not fray. The cut ends of the braided tubular grafts were coagulated slightly wiht the cautery before undertaking the anastomosis in order to prevent fraying of the ends. No oozing of blood took place through the fused nylon-polyethylene grafts or through the methyl-methacrylate-coated graft. In the beginning, unwashed nylon filter fabric grafts were employed, and they did not tend to leak at the time blood was first allowed to flow through them. Experimentally, however, it was found that the results were better when the filter fabric was first washed with a detergent. Such grafts do tend to ooze a little through the interstices of the cloth when blood flow is first established through them. Only in one instance, however, did significant loss of blood occur through the wall of the graft. Such difficulties were obviated by preclotting the external surface of the graft in the

‡ HT-5F Nylon filter fabric. Equipment Development Company, Inc., 368 Bloomfield Ave., Montclair, N. J.

§ Initially supplied by Mr. J. S. Tapp, Research Dept., The Chemstrand Corporation, Decatur, Ala.; later obtained from C. R. Bard, Inc., Summit, N. J.

patient's blood before inserting it or by allowing a little blood to run into the graft after the first anastomosis had been completed, and before the second was accomplished. The Edwards-Tapp braided tubular grafts available to us have varied somewhat in their manufacture and in their tendency to leak blood initially. In general, it was found that this tendency to sweating of blood could be obviated by preclotting the external surface beforehand. In general, the grafts obtained recently have been better in this respect than those secured earlier. Since the first patient was operated upon, there have been available for immediate sterilization plastic grafts of varying size. Whenever an unusual situation has been encountered, a graft of suitable size and shape has been constructed while the operation was progressing. Not infrequently ectasia of the host vessel has necessitated use of a graft of unusual dimensions, larger than any homograft.

In two instances the plastic graft may possibly, though not definitely, have been implicated in the ultimate death of the patient. The first was that of a 64-year-old hypertensive man who had an uneventful excision of a large abdominal aortic aneurysm in May, 1954. A fused nylon-polyethylene graft was inserted between the aorta, above, and the left common iliac and right external iliac arteries, below. One week later he was found to have a very large retroperitoneal abscess, the graft lying completely in a field of pus. The abscess was drained extraperitoneally, and the patient was soon discharged, in good condition. He remained well and had good distal pulses, though he continued to have slight purulent drainage from the sinus tract off and on. Finally, three months later, he began to bleed through the sinus tract and ultimately from the rectum. He repeatedly refused readmission until he was practically moribund; when finally admitted to the hospital, he was oliguric, in profound shock, with an erythrocyte count of 1,340,000, and with very poor circulation to the right lower extremity and marked ischemia of the left lower extremity. At operation a large aneurysm of the left common iliac artery was found. It had ruptured retroperitoneally and into the rectosigmoid. Retrograde thrombosis of the aortic graft had obviously occurred recently from compression, together with distal thrombosis, of the main arterial tree in the left lower extremity. It was not possible to determine from the findings at operation whether the aneurysm had developed from the extensive disease of the left common iliac artery or from a late disruption of the iliac-graft anastomosis. A new aortic-bilateral external iliac graft was inserted, but it was impossible to restore blood flow to the left lower extremity. The patient died some days later, of lower nephron nephrosis. The other case was that of a 78-year-old man operated upon for large bilateral iliac aneurysm. A bifurcation braided nylon tubular graft was interpolated between the aorta and both superficial femoral arteries. In spite of the fact that the graft had been preclotted beforehand, there was more loss of blood through the interstices of the graft than was usually encountered. The right iliac extension of the graft continued to bleed from a number of points for some time. Transfusion of blood had been begun beforehand, and because of the loss of blood multiple transfusions were required. This patient succumbed on the second postoperative day, obviously from a transfusion reaction, with bleeding from the stomach, oral cavity, nose, and rectum. It is possible that the hemolytic transfusion reaction may have begun prior to the difficulty with bleeding from the graft itself. On the other hand, there is a good possibility that the graft itself was at fault and that loss of blood from it necessitated further transfusions, precipitated the transfusion reaction, and was, in effect, the basic cause of the patient's death. The bifurcation braided tubular grafts subsequently procured and utilized seemed far superior to the one under discussion.

There were no instances, I believe, in which the type of graft could be implicated in a definite or probable graft failure. In the case of the 73-year-old man with thrombotic occlusion of his aortic-iliac aneurysm and distal thrombosis, it was impossible to obtain any open arterial pathway into which the graft could empty. Obviously, no graft could have worked under such circumstances. In one patient with partial occlusion of the aorta, complete occlusion of both common iliac and superficial femoral arteries, with no open distal pathway, and with diseased and narrowed external iliac and common femoral arteries, operation was probably undertaken inadvisedly. In this case, bilateral Edwards-Tapp by-pass grafts were interpolated between the aorta and the external iliac arteries. Though the patient feels definitely improved, it is probable that the grafts did not remain open. It is difficult to imagine that another type of graft would have worked in this situation. A patient with an ischemic ulcer of the right ankle and a history of a severe myocardial infarction was, unfortunately, operated upon after a very difficult induction. A bifurcation braided tubular by-pass graft was inserted between the aorta and one popliteal and one femoral artery. The graft to the popliteal artery functioned nicely. The graft to the femoral artery, which was accomplished last, was not functioning adequately at the completion of the anastomosis. Because of the fact that the patient was taking his anesthetic so poorly, the operator elected to close rather than to take down the anastomosis and do it over. The aortic-popliteal side of anastomosis continued to function well, but there were no distal pulses on the other side. This patient, unfortunately, died of aspiration pneumonitis and represents the only fatality in the group of cases operated upon for obliterative disease. From other experiences it seems almost certain that had the patient's general condition warranted redoing of the inadequate graft-femoral anastomosis, success could have been achieved.

In two instances a later partial failure of a graft occurred as the result of an inadequate outflow tract or during a period of hypotension. A 62-year-old man had an abdominal aortic aneurysm and distal obliterative disease of the midsuperficial femoral and popliteal arteries, beyond which there was no patent major artery. Both feet were ischemic, and operative treatment was undertaken with the realization that there was very real risk of further impairing the circulation. At operation both common iliac arteries were found to be obliterated down to the point of bifurcation. The internal iliacs (hypogastrics) were badly diseased and the external iliac arteries nearly totally occluded. The aneurysm was excised, and a graft was placed between the aorta and both superficial femoral arteries, the distal end of both common iliac arteries being closed by suture so as to preserve any possible retrograde flow that might take place through the nearly occluded external iliac arteries into the internal iliacs. Both grafts functioned well for a time, but the patient began to have ischemic pain in the left leg and foot, and, in spite of absence of gangrene in the affected foot, amputation was ultimately required. A bilateral sympathectomy had been done at the time of the initial operation. A 69-year-old patient with a ruptured abdominal aortic aneurysm underwent a resection of the aneurysm and interpolation of a nylon filter fabric graft with an Edwards-Tapp extension between the aorta and the right common iliac artery and the left superficial femoral artery. He did well until his wound eviscerated, on the fourth postoperative day. Following repair of the evisceration, he developed extensive pulmonary atelectasis and five days later went into a state of shock. During this period of pronounced and prolonged hypotension, the extension of the graft to the superficial femoral artery became thrombosed. He died of atelectasis a week later. The remainder of the graft continued to function well until the time of death. It is entirely likely that any other type of aortic-femoral graft might have become oc-

cluded during this period of marked circulatory collapse. Thrombosis of a major arterial stem not infrequently occurs during such episodes in patients with extensive arteriosclerotic disease in the absence of any previous surgery. Furthermore, I have observed two instances in which, during a period of hypotension, distal arterial thrombosis has occurred with maintenance of good circulation through both limbs of the graft.

One patient was a 64-year-old man with hypertensive cardiovascular disease who underwent uneventfully resection of an abdominal aortic aneurysm and interpolation of a nylon filter fabric aortic-bilateral common iliac graft. One week later, for some unexplained reason, he went into profound shock and during this episode developed thrombosis of the external iliac artery distal to the graft. On reexploration the aortic graft and both the iliac extensions were found to be patent. A new graft was interpolated between the aorta and one common iliac and the other femoral artery, with restoration of excellent circulation. The other was a 74-year-old hypertensive woman who had resection of an abdominal aortic aneurysm with insertion of an aortic-bilateral common iliac graft. In spite of adequate blood replacement, her blood pressure, formerly running at high hypertensive levels, remained within the normal range for a number of days. During this period of prolonged relative hypotension, she underwent thrombosis of one superficial femoral artery and maintained excellent circulation through the graft. The common femoral artery on the affected side continued to pulsate nicely. She ultimately required a leg amputation and has remained well for over a year.

During the course of this study it became apparent from experimental observations that nylon filter fabric grafts were far superior to the thin nylon fabric grafts fused with polyethylene or coated with methyl methacrylate. In spite of the fact that the clinical results with the latter grafts were good, nylon filter fabric grafts have since that time been used instead for aortic and aortic-bifurcation replacement. Initially, when grafts had to be extended from the aorta to one femoral artery, the straight braided nylon tubular grafts were joined to the iliac extension of a filter fabric graft. Though they worked satisfactorily, once bifurcation braided tubular grafts became available, the latter were used instead whenever the graft had to be extended from the aorta to a femoral or popliteal artery.

An experience with one of my patients demonstrates clearly the role of the plastic material itself in lending strength to the new blood vessel which the host builds about it. The patient was first operated upon in October, 1953. A large abdominal aortic aneurysm was excised, and a fused nylon and polyethylene graft was sutured in place between the aorta and the proximal portion of both common iliac arteries. He did quite well for a period of 22 months and then was readmitted to the hospital following the sudden onset of ischemia in the right lower extremity. It was obvious from examination that he had undergone an occlusion of the right common iliac artery. The patient was very reluctant to be operated upon, and permission could be secured only by assuring him that this operation would prove much simpler than the first, and would probably require only opening the affected artery and removing the occluding thrombus from it or inserting a relatively short graft. At operation the new aorta which had been laid down about the plastic material was not dilated. It was indeed quite difficult to tell by inspection and palpation from a perfectly normal aorta and its bifurcation. Distally there was a slight dilatation of the right common iliac artery, which pulsated down to its bifurcation, where it was completely occluded by a fresh thrombus superimposed upon an old encircling calcified plaque. The left common iliac artery had undergone moderate dilatation distal to the graft. In removing the diseased intima and the fresh thrombus

superimposed upon it, I began a thromboendarterectomy, which was inadvertently extended too far proximally. Finally, the plastic lining of the iliac extension was separated from the outer fibrous coat. Since I was unable to secure it back in place by suture, as a last resort I ultimately freed the entire plastic lining from the aorta and the proximal portion of both iliac arteries and removed it through the arteriotomy in the right common iliac artery. If I had not promised the patient that I would perform only a relatively simple procedure, I should obviously have resected the aorta and both iliacs and substituted a new graft. Under the circumstances, I did nothing more. The patient had excellent reestablishment of blood flow into his right lower extremity, and he was watched carefully thereafter. Finally he was readmitted to the hospital, in December, 1955. The aorta and its bifurcation, which had remained perfectly normal in size and appearance for approximately two years, had dilated into a large aneurysm during the brief interval following removal of the plastic lining. The patient was reoperated upon, and it was possible to resect the aneurysm and interpolate a new filter fabric graft. He has done well during the 14 months which have elapsed since that time. This experience demonstrates, I feel, the importance of the plastic fabric in lending strength to the new blood vessel built about it by the host. It certainly suggests equally strongly that unless the elastic layer of the homograft persists as a strength-giving membrane, new blood vessels built about homografts will also inevitably undergo dilatation. Thus far, our clinical and experimental experiences give no indication that the plastic grafts used fail to continue to provide the new vessel with adequate strength.

I have previously mentioned that two patients ruptured the aorta, one and four months, respectively, proximal to the aortic graft anastomosis. From postmortem study in one case and from examination of the excised surgical specimen in the other, it was clear that perforation had occurred from 1 to 2 cm. proximal to the intact and healed aortic graft anastomosis, and precisely at the level at which the aorta had been cross-clamped with a Pott's clamp. Since then, we have utilized a new clamp,‖ the blades of which are approximated by a screw-down mechanism, which permits one to tighten the blades of the instrument just sufficiently to bring about occlusion of the artery.

Comment and Summary

My experiences with the use of plastic grafts for aortic replacement and for bypass grafting between the aorta and its tributaries have proved altogether satisfying. As a result of them, at the present time I am employing nylon filter fabric grafts whenever a segment of the thoracic or abdominal aorta must be replaced, or the abdominal aorta and its bifurcation. When grafts must be interpolated between the aorta and the peripheral arteries in the lower extremities, it is my policy to use the Edwards-Tapp nylon grafts. I should utilize by preference a homograft if numerous branches of the aorta required anastomosis, as is the situation in replacing the upper abdominal aortic segments.

It is entirely possible that better plastic grafts will be available in the future. Certain experimental studies would indicate that nylon tends to lose strength during the first months after implantation to a greater degree than do some other plastic materials, such as Dacron and Teflon. From our clinical and experimental evidence, it would seem that the initial strength of nylon grafts such as we have used is so great that, in spite of any initial loss of strength, the grafts ultimately are quite strong enough to prevent dilatation or aneurysmal formation.

In the 92 cases reviewed there was one possible case in which rather prolonged and troublesome bleeding through a bifurcation Edwards-Tapp graft may have been

‖ Made by George P. Pilling and Son Company, 3451 Walnut St., Philadelphia 4.

responsible for the patient's death. It is my impression that the quality of this particular type of graft has improved considerably since this experience took place. The one possible instance of graft-iliac suture line disruption occurred in the case in which the graft lay in an infected field. It is difficult to believe that a homograft would have behaved better under these circumstances. Careful consideration of the few instances of definite or probable graft failure lead me to believe that the same outcome would likely have prevailed had another type of graft been utilized. With these few exceptions, the grafts have worked well. In those cases in which grafts have been in place for several years, there is every evidence to suggest that they are functioning well without dilatation or stenosis.

I believe that years must pass by before we shall have objective evidence to permit us properly to evaluate the relative merits of plastic vascular substitutes, on the one hand, and homografts, on the other. At the moment it seems fair to conclude that certain plastic grafts are entirely suitable in the hands of those experienced in their use for aortic substitution.

1040-1232 W. Michigan St. (7).

Addendum

Since submission of this paper for publication I have continued to employ nylon filter fabric grafts and the straight tubular crimped Edwards-Tapp grafts, with satisfaction. The tendency toward oozing of blood through the bifurcation Edwards-Tapp grafts has, however, made me reluctant to use them further.

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DISCUSSION

DR. ORMAND C. JULIAN, Chicago: I want to comment on how closely my experiences parallels those of Dr. Shumacker. In regard to replacement of the thoracic aorta and the aortic bifurcation only, there is emphasis to be placed on one of the advantages and one of the disadvantages which he has mentioned.

An outstanding advantage of prostheses in aneurysm surgery is the availability of a variety of sizes, which, of course, does not apply to the use of homografts. My colleagues and I have used a bifurcation made of Dacron that can be made in a variety of sizes and is preformed by the manufacturer. It is rare to encounter an aneurysm in either location in which a perfect fit cannot be obtained by one of these bifurcations or straight tubes. The advantage of having them preformed, of course, is that one does not need a sewing machine after the measurements have been taken.

A disadvantage which has been encountered once in some 60 cases of Dacron replacement of aneurysms in a series of Deterling's in New York, and of our own, in Chicago, was a severe episode of bleeding through the graft. In this case, after the graft had been in place for a few minutes and was completely impervious to blood, the wound

began to ooze from all surfaces. In this patient the entire surface of the graft then began to bleed. We lost the patient because of the impossibility of controlling the hemorrhage through the graft.

We think that the development of fibrinolysins or some other enzyme system probably accounted for the dissolution of the fibrin that had already been laid down in the interstices of the graft, and in this case caused the patient's death.

DR. HARRIS B. SHUMACKER JR., Indianapolis: The point that Dr. Julian mentioned is quite apropos. In general, we have not had any difficulty with bleeding through the nylon filter fabric grafts, with which we have had our largest experience. We have had some oozing through the Edwards-Tapp type of graft, but I think the product has steadily improved, and, except for one case which I mentioned, we have had no serious difficulty.

We did, however, have one case somewhat like that mentioned by Dr. Julian. The patient had no initial leak through the graft, and the operative field seemed relatively dry. Shortly thereafter he began to bleed profusely from various points, and at the same time began then to leak through the nylon filter fabric graft. With hot packs we were able to control this bleeding, but the patient died of cardiac arrest not long thereafter. Such occurrences must be relatively rare. Perhaps, as Dr. Julian intimated, they are related to some minor or major transfusion reaction.

Clinical Appraisal of Percutaneous Splenoportography

MARION S. DeWEESE, M.D.; MELVIN M. FIGLEY, M.D.; WILLIAM J. FRY, M.D.; ROBERT RAPP, M.D., and HOWARD L. SMITH, M.D., Ann Arbor, Mich.

The pathologic anatomy of the portal venous system as it is associated with various diseases of the upper abdomen has assumed increasing importance in recent years. As a clearer understanding of the mechanisms involved in the production of portal hypertension has developed [22] and as experience with the reduction of portal venous pressure by shunting procedures has accumulated,[7,16] accurate techniques for the preoperative evaluation of existing abnormalities of this venous system have become more necessary. This report is concerned with our experiences with one of these procedures, percutaneous splenoportography, in 120 patients examined over a period of three and a half years. Of these, 93 were patients in the University Hospital, and 27, in the Veterans' Administration Hospital, Ann Arbor.

Radiographic visualization of the portal venous system by direct injection of contrast material into a tributary of the portal vein at the time of laparotomy has been used advantageously by a few surgeons since 1945.[6,9,17,19] General application of this method of study has been discouraged, however, by the lack of suitable safe radiologic equipment in most operating rooms. It also entails the loss of valuable time during an operation, which is usually long and tedious. Neither does it permit careful preoperative evaluation of important radiographic evidence in conjunction with the clinical and laboratory data upon which the decision for operation is based.

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From the Departments of Surgery and Radiology, University of Michigan Medical School, and the Veterans' Administration Hospital.

In 1942 Blalock observed that contrast material injected into an abdominal sinus tract of a patient had by chance entered the portal venous circulation through the spleen. This serendipitous observation led to laboratory studies, and, as reported by Bahnson, Sloan, and Blalock in 1953,[5] percutaneous splenoportography was performed clinically at The Johns Hopkins Hospital as early as 1949.

Meanwhile considerably greater enthusiasm was arising in Europe for the utilization of the unique vascular structure of the spleen as a means of access to the portal venous circulation. De Sousa Pereira [11] injected contrast media directly into the spleen at laparotomy, as well as into the mesenteric veins, and obtained satisfactory portal venograms in 1951. In the same year, Abeatici and Campi reported both laboratory [1] and clinical [2] experiences with the percutaneous route, although Leger,[15] stimulated by these investigators, first reported the successful accomplishment of percutaneous splenoportography in a patient. A number of favorable reports have appeared since that time, but the procedure has been accepted reluctantly in this country. Following the encouraging experience of Cooper and his co-workers in 1953,[10] we initiated this clinical appraisal of the method.

Technical Considerations

The technique which we have employed is similar to that used by Abeatici,[2] Dreyer,[12] and Sotgiu,[20] and was described by Figley [13] in a previous report from this center. We now employ an intercostal approach in all patients and use 70% sodium acetrizoate (Sodium Urokon) as a contrast medium.

We consider it mandatory that all patients be hospitalized and that all other pertinent diagnostic studies be completed before splenoportography is undertaken. Liver function tests, upper gastrointestinal x-rays, and hematologic survey for evidence of hypersplenism are done in those patients with suspected portal hypertension. Prothrombin deficiencies are corrected and the patient prepared for definitive operation. If there is no demonstrable bleeding tendency, we prefer to carry out the examination in the radiology department one or several days prior to operation. The patients are well premedicated, and local anesthesia is employed except in young children. We follow the same procedure if the patient is a poor operative risk or has a noncorrectible bleeding tendency, but perform the examination just prior to operation, on the same day. Although splenic hemorrhage has not been a serious problem, its occurrence might compromise the success of a shunting procedure. We believe that these measures are only prudent.

An automatic filming device permitting serial exposures at the rate of 1.3/sec. has been utilized in three-fourths of these examinations. Although it is a helpful technical refinement, it is not essential to the success of the procedure, as many satisfactory examinations have been accomplished by rapid manual changing of the cassettes.

In our over-all experience, one or more successful examinations have been completed in 103 of the 120 patients in whom it has been attempted (85.6%). Multiple examinations have been successfully completed in some of these; in others reexamination after initial failure has resulted in success. A total of 134 examinations have been attempted, of which 113 have been successful (84.3%). The technical quality of the examination was good in 70.1% and gave us essentially all the information that we feel is obtainable by the method. The examination was of substandard quality in 14.2% but gave us some help in clarifying the clinical problem in most of these cases. The remainder, 15.7%, were complete failures.

The cause of failure in 15 attempts was either our inability to position the needle within the spleen or retrograde extravasation of contrast material along the needle tract after it had entered the spleen rather than passing into the portal circulation. Acetrizoate has been injected into the free peritoneal, pleural, or retroperitoneal spaces in nine of these patients, without ill effect other than transient discomfort. Subcapsular splenic injection due to poor positioning of the needle or retrograde extravasation has also been accompanied by increased pain. As our experience with the technique has increased, these failures have become fewer. A test injection of acetrizoate preceding the definitive injection has greatly aided in proper positioning of the needle. Recently we have advantageously employed a needle with a lateral fenestra to reduce the retrograde extravasation of contrast material during its injection under pressure.

Three examinations were unsuccessful because of untimely failure of the x-ray tube. These accidents are difficult to eliminate, as the tube is heavily loaded, particularly with the use of the automatic serial filming device in obese patients. Manual cassette changing is probably preferable in heavy patients. In other instances, technical difficulties with the radiologic equipment have been immediately corrected and the injection has been repeated successfully. These have not been considered failures.

Three examinations resulted in failure because of nontransit of contrast media from the spleen after a satisfactory puncture in patients who had no evidence of splenic vein occlusion. This is a disturbing phenomenon, as it simulates findings sometimes observed in patients with neoplastic occlusion of the splenic vein.

Complications

We have had no deaths attributable to the procedure, and in no patient have we been forced to perform emergency splenectomy because of hemorrhage, though such a

complication has been reported.[18] One patient with unrecognized thrombocytopenia did develop evidence of intra-abdominal hemorrhage and required transfusion of 1500 cc. of blood to combat shock. She responded to conservative measures and later underwent elective operation uneventfully. This is the only patient who has presented clinical evidence of blood loss after the procedure.

Eighty-five of the one hundred twenty patients have undergone laparotomy subsequent to successful or unsuccessful splenoportography. Although operative notes are notoriously devoid of important information, in only six was there sufficient free blood in the peritoneal cavity to invite comment. The estimated volume in these few was 100-300 cc. Although this figure is admittedly not a true reflection of the probable incidence of mild splenic bleeding following the puncture, much of our fear of catastrophic hemorrhage has been dispelled. We do feel that it is a constant potential hazard, however, and exert rigid precautions to prevent its occurrence or to protect the patient if it should occur. Thrombosis of the splenic or portal vein has not, to our knowledge, resulted from the procedure. Pneumothorax developed incident to the transthoracic splenic puncture in two cases, in one of which intervention was required. In another case pleuritis developed several days after an otherwise uncomplicated procedure, in which there was no radiographic evidence of intrapleural injection of acetrizoate. The mechanism of this was obscure, but it must be accepted as a complication of the procedure. None of these patients experienced prolonged morbidity.

There have been some disturbing symptoms associated with the examination which cannot be classed as true complications. Transient abdominal or shoulder pain has been noted in about half of the patients. A relative few have had transient nausea, flush, or hypotension attributable to the contrast material. Catastrophic allergic reaction is a potential hazard in this examination, just as in any other which requires the use of intravenous contrast media; but, fortunately, none has occurred. It is our impression that this examination is no more disturbing to patients than are most endoscopic or angiographic diagnostic procedures.

Radiologic Interpretation

It is not the purpose of this communication to describe the radiographic interpretation of splenoportograms in detail, although some basic observations must be mentioned. In the normal subject (Fig. 1) the bolus of contrast material leaves the spleen and passes rapidly through the splenic and portal veins and the intrahepatic portal ramifications. Finally a diffuse haziness of the liver parenchyma, known as the hepatogram, is observed, followed by rapid clearing of the contrast medium. The entire cycle is usually completed in less than 20 seconds. Normally there is no fill of collateral channels or portal vein tributaries, although there may occasionally be a transient reflux for a short distance into the larger tributaries as the contrast medium is injected under pressure.

In portal hypertension from any cause, there is reverse flow of varying degree into the tributaries and collateral channels of the portal vein. The superior mesenteric,

Fig. 1.—Normal splenoportogram.

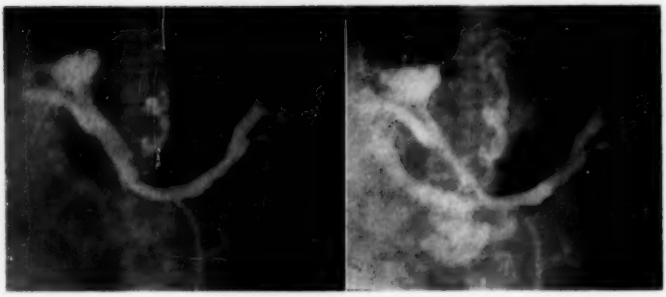

Fig. 2.—Intrahepatic portal obstruction, with esophageal varices and patent umbilical vein (Cruveilhier-Baumgarten syndrome).

inferior mesenteric, coronary, short gastric, and esophageal veins, among others, may be outlined. In certain situations the veins of Retzius or of Sappey may be seen, and, in the Cruveilheir-Baumgarten syndrome (congenital cirrhosis of the liver), the umbilical vein can be identified (Fig. 2).

Cirrhosis of the liver may be suspected on the basis of radiographic evidence of abnormalities in the size of the liver, crowding or tortuosity of the larger venous branches within the liver, or attenuation of the peripheral branches. The diagnosis of portal hypertension of intrahepatic origin is made on the basis of visualization of collateral channels, patency of the splenic and portal veins, and, less importantly, the radiologic evidences of cirrhosis mentioned above. These observations must, of course, be correlated with clinical findings and with laboratory evidence of disturbances in liver function.

Extrahepatic portal obstruction associated with cavernomatous transformation of the portal vein (Fig. 3) is revealed by multiple tortuous channels in the region of the hepatoduodenal ligament, through which the contrast medium eventually reaches the liver. This is accompanied by filling of the collateral channels, indicating portal hypertension. The diagnosis of portal hypertension due to hepatic vein obstruction (Chiari-Budd syndrome) cannot be made with finality on the basis of splenoportography but may be suspected on the finding of a patent portal vein, distended collateral channels, and normal intrahepatic branching of the portal vein in the presence of normal liver function.

Intrahepatic neoplasms produce blunting of the larger portal branches within the liver or mottled densities in the hepatogram. Extrahepatic neoplasms may produce filling defects of the portal or splenic veins, or complete block, with filling of collateral channels distal to the point of obstruction (Fig. 4). Complete obstruction of the splenic vein by neoplasms in the tail of the pancreas may produce nontransit of the contrast medium from the spleen, but this must be evaluated carefully, as it has also been observed in apparently normal patients.

Fig. 3.—Extrahepatic portal obstruction with cavernomatous transformation of portal vein and esophageal varices.

Fig. 4.—Pancreatic cyst producing distortion and partial obstruction of splenic vein and distended collateral veins distally.

Analysis of Material

In an effort to assay the areas of clinical usefulness of percutaneous splenoportography, the 103 patients examined successfully thus far have been placed in five clinical groups. All available clinical and laboratory information, including findings at operation and at autopsy, have been called upon in an attempt to establish an accurate diagnosis in each. Laparotomy was performed in 72 of these patients, and tissue for histologic study was obtained in 12 others by autopsy, liver aspiration, endoscopy, or incisional biopsy of extra-abdominal primary or metastatic malignant lesions.

GROUP 1: *Portal Hypertension and/or Cirrhosis* (47 patients; Table 1).—Twelve patients presented with clinical evidence of cirrhosis and esophageal varices, as proved by previous esophagography or esophagoscopy. Percutaneous splenoportography confirmed the diagnosis of portal hypertension of intrahepatic origin in all 12, and the esophageal varices were clearly demonstrated in 9. There were no "false" normals in the group.

Ten patients were examined because of clinical evidence of cirrhosis and a history of upper gastrointestinal hemorrhage. Esophageal varices had not been previously demonstrated by standard diagnostic methods in any of these, although presumably some might have been had conventional studies been pursued more diligently. Varices were unequivocally demonstrated by splenoportography in five patients, one of whom was also found to have patency of the umbilical vein (Cruveilhier-Baumgarten syndrome). The presence of visible collateral channels supported the diagnosis of portal hypertension in one other. Varices were effectively ruled out as the cause of bleeding in the two reported as normal. Some variations in the intrahepatic portal branching, supporting the diagnosis of cirrhosis, were present in both. Bleeding was later found to be due to a gastric ulcer in one of these patients and to hypertrophic gastritis in the other. The quality of the splenoportogram was substandard in the two additional patients and did not permit more precise diagnosis, although the patency of the splenic and portal veins was established in them as well as in the others.

Percutaneous splenoportography was performed in 15 patients with cirrhosis who had no history of gastrointestinal bleeding and in whom varices had not been demonstrated by other methods. Varices were detected by this method in three and collateral channels were visualized in five others, thus confirming the presence of some

TABLE 1.—*Appraisal of Percutaneous Splenoportography: Portal Hypertension and/or Cirrhosis*

Clinical Entity	No.	Splenoportographic Findings			
		Varices	Other Collaterals	Patent Portal Vein	Normal ("Cirrhosis")
A. Cirrhosis + known varices	12	9	3	12	0
B. Cirrhosis + bleeding; neg. G. I. x-ray	10	5	1	10	2
C. Cirrhosis; no bleeding; neg. G. I. x-ray	15	3	5	15	4
D. Extrahepatic portal obstruction	10	6	4	1	6
Total	47	23	13	38	6

Fig. 5.—Splenoportogram of patent portacaval shunt (arrows indicate vena cava).

degree of portal hypertension in eight; the diagnosis of Cruveilhier-Baumgarten syndrome was established in two. Patency of the portal system was demonstrated in all, as were intrahepatic venous aberrations, which supported the diagnosis of cirrhosis.

Extrahepatic portal hypertension was proved in 10 patients who were examined because of splenomegaly and previously demonstrated esophageal varices or a history of upper gastrointestinal hemorrhage. Nine of these patients were found to have thrombosis or cavernomatous transformation of the portal vein (Smith-Howard syndrome). The other had hepatic vein obstruction due to an intrathoracic tumor. All 10 patients were shown by splenoportography to have portal hypertension, as evidenced by visualization of esophageal varices or other collateral channels.

Postoperative visualization of a portacaval shunt was attempted in six patients. Patency of the shunt was unequivocably demonstrated by this method in four (Fig. 5) and occlusion of the shunt in another. The examination was of substandard quality in the sixth patient but supported a presumptive impression of patency.

Group II: *Neoplasms of Liver* (20 patients; Table 2).—Primary and metastatic lesions of the liver are considered in this group. The primary group includes one patient with benign hepatic cyst, one with carcinoma arising in the gallbladder, and two with primary malignant neoplasms of hepatic-cell origin. One patient had lymphoblastoma involving the liver, as well as other abdominal organs.

The metastatic neoplasms had originated in the esophagus, stomach, pancreas, colon, rectum, and lung. Most patients presented with a palpable abdominal mass or visualization of extrinsic pressure defects by standard gastrointestinal x-ray. The splenoportograms provided the only objective evidence of hepatic metastases in five patients, in three of whom the diagnosis was confirmed at operation.

Positive splenoportographic evidence of an intrahepatic space-filling lesion was found in 13 of the 20 patients in this group; 9 of the 13 were verified by laparotomy. Extrahepatic compression of the portal vein was observed in four. The findings were considered equivocal at the time of the examination in two of these but were later proved to be valid, as was one of the two thought to be unequivocal. Distention of collateral portal venous channels was the only abnormal finding in one, the patient with primary carcinoma of the gallbladder. There was one "false"-normal examination in a patient who was later found to have multiple small hepatic metastases. The other patient with a normal splenoportogram had an in-

Table 2.—*Appraisal of Percutaneous Splenoportography: Neoplasm of Liver*

Clinical Entity	No.	Splenoportographic Findings			
		Intrahepatic Abnormality	Extrahepatic Abnormality	Collaterals	Normal
A. Primary—proved	5	3	1	1	0
B. Metastatic—proved	9	6	2	0	1
C. Metastatic—not proved	6	4	1	0	1
Total	20	13	4	1	2

TABLE 3.—*Appraisal of Percutaneous Splenoportography: Lesion of Pancreas*

Clinical Entity	No.	Splenoportographic Findings			
		Intrahepatic Abnormality	Extrahepatic Abnormality	Collaterals	Normal
A. Chronic pancreatitis	1	0	1	..	0
B. Pancreatic cyst	3	0	3	..	0
C. Carcinoma, head	3	0	1	..	2
D. Carcinoma, body or tail	3	..	3*	..	0
Total	10	0	8	..	2

* Nontransit in two.

operable carcinoma of the lung. Hepatic metastasis was suspected on the basis of an extrinsic pressure defect in the upper gastrointestinal x-ray, but this was never proved.

GROUP III: *Lesions of the Pancreas* (10 patients; Table 3).—Percutaneous splenoportography provided interesting and helpful findings in this group of patients. Cysts or pseudocysts were uniformly well demonstrated. All three patients with carcinoma of the body or tail of the pancreas also had abnormal findings. In two of these, whose lesions totally obstructed the splenic vein, there was complete nontransit of contrast medium from the spleen, a finding which must be evaluated cautiously, as previously stated. Only one of three patients with obstructive jaundice due to carcinoma of the head of the pancreas had abnormal splenoportographic findings. This patient was the only one of the three with a palpable abdominal mass; but only palliative operations were possible in all three.

GROUP IV: *Other Malignant Lesions* (9 patients; Table 4).—Seven patients with advanced intra-abdominal carcinomatosis were examined. Two of these had clinically palpable abdominal masses, and four had extrinsic pressure defects visible in standard gastrointestinal x-rays. Five of the patients had positive splenoportographic findings and were proved to have advanced primary carcinomas of the stomach or recurrent lesions of the stomach or head of the pancreas. Two patients with normal splenoportograms had diffuse peritoneal carcinomatosis from undetected primary lesions.

The two patients with retroperitoneal neoplasms had no abnormalities on this examination, as might be anticipated.

GROUP V: *Other Benign Lesions* (17 patients; Table 5).—Although they presented diagnostic problems at the time of splenoportography, all the patients in this group were later proved to have benign lesions. All but one had normal splenoportograms.

Of the two patients with upper gastrointestinal hemorrhage, examined on the suspicion of esophageal varices, one was subsequently found to have peptic esophagitis and the other severe alcoholic gastritis. Two of the patients with jaundice, examined on the suspicion of pancreatic neoplasm, were later found to have common duct stones. Hepatitis was subsequently discovered to be the cause of jaundice in the other patient, but splenoportography had no apparent adverse effect.

One of the patients with hepatosplenomegaly was found to have lipid histiocytosis of Kerasin type (Gaucher's disease), and another, miliary tuberculosis. The examination helped rule out a neoplastic lesion in

TABLE 4.—*Appraisal of Percutaneous Splenoportography: Other Malignant Lesions*

Clinical Entity	No.	Splenoportographic Findings			
		Intrahepatic Abnormality	Extrahepatic Abnormality	Collaterals	Normal
A. Abdominal carcinomatosis	7	1	4	..	2
B. Retroperitoneal neoplasm	2	0	0	0	2
Total	9	1	4	0	4

TABLE 5.—*Appraisal of Percutaneous Splenoportography: Other Benign Lesions*

Clinical Entity	No.	Splenoportographic Findings			
		Intrahepatic Abnormality	Extrahepatic Abnormality	Collaterals	Normal
A. G. I. bleeding; no cirrhosis	2	0	0	0	2
B. Jaundice; no cirrhosis	3	0	0	0	3
C. Hepato—and/or splenomegaly	5	0	0	0	5
D. Rupture, liver or gallbladder	2	1	0	0	1
E. Anorexia, ascites	5	0	0	0	5
Total	17	1	0	0	16

another patient with associated hepatomegaly and acute thrombophlebitis.

Abnormal density of a localized area in the hepatogram was observed in a patient with a bizarre history of ascites developing subsequent to abdominal trauma sustained seven weeks previously. A laceration of the liver was found at operation. Another patient with traumatic rupture of the gallbladder had a normal splenoportogram.

The remaining patients presented with nonspecific complaints of anorexia, weight loss, or abdominal pain. They were examined upon the suspicion of obscure intra-abdominal neoplasms, and the negative findings were consistent with the subsequent findings or clinical course.

We believe it significant that there were no false-positive findings in this group of patients.

Splenic Pulp Pressures.—Following a report by Atkinson and Sherlock,[3] which pointed out the close correlation between portal venous pressure and splenic pulp pressure, an attempt has been made to measure splenic pulp pressure simultaneously with the performance of percutaneous splenoportography. This has been accomplished in 17 patients. In many instances the splenic pressures have paralleled the direct portal pressures and have been consistent with the splenoportographic findings. We have, however, experienced some technical difficulties in carrying out the procedures simultaneously which have resulted in inaccuracies and inconsistencies. In general, it appears to us that the information to be derived from the splenoportogram is more comprehensive and reliable than is that to be obtained from the splenic pulp pressure, but that both should find an ultimate field of usefulness.[3,14]

Comment

In the course of this study we have attempted to define the field of usefulness of percutaneous splenoportography and have doubtless employed it on occasions in which conventional studies would have served equally as well. It is most certainly not a diagnostic panacea for all obscure problems arising in the upper abdomen. We believe, however, that if properly utilized it can be an important method of study.

The infrequency of complications, particularly in respect to splenic hemorrhage, has dispelled many of our early apprehensions about the safety of this method. Most other writers report a similar experience.[8,10] Although complications can occur, they need not be prohibitive if proper precautions are taken in the selection and preparation of the patient and in the performance of the examination.

We are particularly enthusiastic over the diagnostic aid that splenoportography has provided us in the evaluation of patients with suspected portal hypertension. We cannot agree with Linton[16] that the complications are prohibitive or that the examination fails to impart information that is always accurately obtainable from clinical or laboratory evidence.

Esophageal varices have been visualized in a high percentage of the patients in which they were proved to be present. This is not the chief value of the procedure, however, as carefully performed esophagograms should disclose varices equally as accurately

when they exist. Splenoportography does provide more direct and comprehensive information regarding the pathologic anatomy of the portal venous system than is obtainable by any method other than direct portal venography. In our opinion, this constitutes the chief justification for its use.

Whenever it is feasible, we prefer a direct portacaval shunt in the surgical treatment of portal hypertension. Extrahepatic occlusion or cavernomatous transformation of the portal vein, or well-advanced secondary hypersplenism has been our chief indication for the selection of a splenorenal anastomosis. In no instance has successful splenoportography failed to give us reliable preoperative evidence regarding the patency of the splenic and portal veins.

The procedure has helped clarify the etiology of portal hypertension in a number of patients whose clinical findings have been confusing to us. Although normal liver function in the presence of esophageal varices is highly indicative of extrahepatic block, abnormal liver function and extrahepatic obstruction do coexist.

Neither is the age of the patient a reliable indication of the site of block. The average age of patients in this series with intrahepatic portal obstruction was 34 years; the age of those with extrahepatic obstruction averaged 32.1 years. Oddly enough, the youngest patient with each type of obstruction was 3 years of age, and, by further coincidence, the oldest patient in each group was 62 years old.

Percutaneous splenoportography has also provided a direct, generally available visual method of determining the patency of a direct portacaval shunt postoperatively. We believe this to be an important use for the procedure. Although theoretically the contrast material might conceivably induce thrombosis of the splenic or portal vein, or of the shunt, we have not observed any evidence that this is a justifiable concern.

The wisdom of withholding a shunting operation from patients with known portal hypertension until massive hematemesis occurs has recently been challenged.[21] We have been impressed by the frequency with which unsuspected varices or other evidences of occult portal hypertension have been disclosed by splenoportography in patients with cirrhosis. The proper management of such patients is controversial and largely dependent upon other factors at this time, but splenoportography can be very useful in assessing the status and progression of the disease. Splenic pulp pressures may also be helpful but in our opinion can best be used to supplement the information provided by radiographic visualization.

Although the diagnosis of uncomplicated cirrhosis of the liver is more properly made on the basis of clinical and laboratory evidence, splenoportography can on occasion support the diagnosis. It has provided the first indication of cirrhosis in a small number of these patients, though we do not propose that it is an important area of usefulness for the procedure.

Percutaneous splenoportography has been of distinct help in visualizing hepatic tumors and other neoplasms of the upper abdomen, particularly those arising in the tail or body of the pancreas. It is subject to some limitations when used for this purpose, as operation is frequently necessary anyway to establish histologic characteristics or prognosis in those patients in whom tumors are visualized. It should probably be reserved for those in whom obscure upper abdominal neoplasms, not identifiable by other nonoperative diagnostic measures, are suspected. It may also be useful in detecting hepatic or intra-abdominal metastases in patients with such primary neoplasms as carcinoma of the breast or lung, in whom the presence of metastases may importantly influence palliative therapy.

The procedure would seem to have little or no place in the differential diagnosis of jaundice. Our experience with splenoportography in patients with carcinoma of the head of the pancreas is small but discouraging. It would seem doubtful that such lesions can be consistently detected by this technique

sufficiently early to influence their management. Other surgical lesions which produce jaundice are also outside the limitations of the method.

The procedure has helped clarify the diagnosis in many patients with upper gastrointestinal bleeding, but we have not felt justified in subjecting patients to the examination during an episode of massive hemorrhage. Percutaneous splenoportography has been helpful in other situations, but the indications for its use in these must be determined on an individual basis after careful study by conventional methods.

Summary and Conclusions

Percutaneous splenoportography has been completed successfully in 84.3% of the 134 examinations attempted in 120 patients.

Complications of the procedure have not been prohibitive. Serious splenic hemorrhage has occurred in one patient (0.75%). None has required emergency splenectomy.

The procedure has little value in the differential diagnosis of jaundice.

It is sometimes of aid in the detection of obscure neoplasms of the liver, pancreas, and upper abdomen.

It is a useful direct method of determining postoperative patency of portacaval shunts.

It is of primary value in the evaluation of patients with portal hypertension, either manifest or occult.

In our opinion, percutaneous splenoportography is a good, relatively safe procedure which deserves wider acceptance as a specialized radiologic examination in properly selected patients.

Department of Surgery and Radiology, University of Michigan Medical School.

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DISCUSSION

DR. M. M. MUSSELMAN, Omaha: I have learned much from this comprehensive report by Dr. DeWeese. We at Omaha have fewer patients and fewer opportunities to use this procedure. Also, we have no means of using an automatic cassette changer or rapid serial films. Still, we have found this procedure helpful and valuable in the management of our patients.

We inject 30 cc. of 70% sodium acetrizoate as rapidly as possible. This takes about four seconds. I think serial films are essential in this examination. Having no automatic film changer, we have two technicians shuttle back and forth between the control booth and the table. The traffic gets pretty heavy at times. They are able to change a film about every three seconds, using the cassette holder on the x-ray table. We take our first film at about the midpoint of injection. We usually get a total of four films.

(Slide) This was a woman who had a hepatic artery ligation several years ago because of portal hypertension. This splenoportogram shows regurgitation of the dye into, and dilatation of, the coronary vein, indicating that she still has portal hypertension.

(Slide) This woman had a large upper abdominal mass. This splenoportogram shows deflection of the splenic vein superiorly. It also shows the general outline of the mass. This was compatible with a pancreatic cyst, and we operated upon the patient for a pancreatic cyst. At operation we found a more unusual lesion, a cyst of the spleen.

I compliment Dr. DeWeese on his excellent presentation of the extensive experience which he and his associates have had in this procedure. I must say that, after his report, I am encouraged and my opinion is reaffirmed that this procedure is a valuable one. We shall continue to use it, perhaps even more than we have.

DR. EDWIN H. ELLISON, Columbus, Ohio: In the past year we have had 52 splenectomies in University Hospital. Three of the patients had extrahepatic portal blocks with patent portal veins.

(Slide) We do our percutaneous injections by the same technique as that described by Dr. DeWeese. Notice in the first case that there is no splenic vein demonstrable in the splenic hilus. The portal system is filling by means of collaterals through two major vessels, namely, the left gastroepiploic and the short gastric veins.

(Slide) In a second patient we almost had reason to explore the abdomen because of the large anomalous collateral vein. Once again the portal vein is filled with dye and the splenic vein is completely absent. An extremely large collateral vein located in the periphery of the omentum is coursing across the lateral aspect of the spleen, and at operation we noted that our needle had missed passing through this vessel by only a hairsbreadth.

(Slide) A third patient proved to be very interesting, inasmuch as she was thought to have a lymphoma after we had found an extremely widened mediastinum.

(Slide) Note the tortuous esophageal varices demonstrated after recovery from a massive hemorrhage.

(Slide) Note the extensive collateral circulation and the dilated varices filled with radiopaque dye. These veins accounted for the extremely large mediastinal shadow.

(Slide) Following splenectomy, the mediastinal shadow returned to normal size.

(Slide) The final patient was referred to the hospital with a diagnosis of carcinoma of the cardia.

(Slide) The irregularity of the stomach wall proved to be due to varices, as shown by percutaneous splenoportography.

In summary, we agree that this procedure is useful in diagnosing extrahepatic obstructions which can be cured by splenectomy.

DR. JACOB K. BERMAN, Indianapolis: I appreciate your invitation to discuss these excellent papers, because they have been informative and indeed timely. A good meeting must have some nonconformists, and I presume that I belong in this group.

We have done a few splenoportograms, but always just prior to surgery. I believe they are helpful in locating abnormalities and the sites of the obstructions in the portal system.

Any artery or vein may be occluded without death of tissue, anatomical part, or organ if the imperforation occurs gradually. This phenomenon, so well described by Harvey over 300 years ago, is known as collateral circulation. We have obstructed every important artery, including the aorta, and every large vein in the dog without fatality when our occluding process has been accomplished in a leisurely manner.

A complete by-pass of an organ is not like a physiological shunt, which communicates with capillaries or sinusoids. Moreover, pressures in vascular beds where artificial shunts are made soon reach their preoperative level.

Artificial shunts do not take the organ or tissue mass into consideration at all. This blood flow simply circumvents the organ. Sinusoidal communications could not function under such conditions were it not for natural collaterals.

When an obstruction is present in a vessel or organ, compensatory mechanisms for the onward transit of blood are seen in one or all of the following patterns: (*a*) terminal collaterals, as seen in the angiomatous transformation in the liver; (*b*) anastomosing plexuses, as exemplified in esophageal varices; (*c*) by-pass collaterals, as evidenced by the communications between the paraumbilicals and superficial abdominal veins and the dilated retroperitoneal plexuses.

If I were using a splenoportogram routinely, I would want to know primarily how much collateral circulation was present. I believe our objectives should include experiments to find better methods of inviting collateral circulation, as well as procedures for circumventing organs and tissues.

Dr. Harris B. Shumacker Jr., Indianapolis: I have enjoyed this paper very much, as well as the discussion which has followed it.

I simply rise to point out that if anyone fears the rare occurrence of hemorrhage from percutaneous splenic puncture and wishes to obtain portal venograms, another method is available. This is a method which I am sure has been used by many of you. It has been employed very successfully in our group by Dr. Frederick Taylor, by me, and by our associates.

If we wish to study a patient prior to operation, we make a very small abdominal incision under local anesthesia, cannulate an omental vein with a small plastic tube, and keep it open with a slow drip of a dilute heparin solution. The patient can then be examined by portal venography in the x-ray department not only once but repeatedly if it is thought desirable. One can also at one's leisure obtain portal pressure studies not only in the horizontal position but in any other position one wishes. It also permits one to study the effect of such stresses as forced abdominal contraction, various respiratory movements, et cetera. We have found this method to be very satisfactory indeed.

Dr. Robert M. Zollinger, Columbus, Ohio: Is that followed by immediate surgery?

Dr. Harris B. Shumacker, Indianapolis: We do these studies and usually operate a day or so later.

Dr. Robert M. Zollinger, Columbus, Ohio: Do you leave the cannula in for a while?

Dr. Harris B. Shumacker, Indianapolis: It can be left in as long as one wishes. Before it is removed, we stop the drip to make sure that a small segment of the cannulated omental vein is thrombosed. We have had no instances of hemorrhage.

Dr. Robert M. Zollinger, Columbus, Ohio: Then you pull out the tube?

Dr. Harris B. Shumacker, Indianapolis: Yes, we then pull out the polyethylene tube.

Dr. William J. Fry, Ann Arbor, Mich.: I should like to present just one slide to show our reasons for failure.

(Slide) We had 12 patients in whom we were unable to puncture the spleen. That was early in the series. On three we did not attempt an injection because we were not sure that the needle was in the spleen, and injected the acetrizoate directly into the intraperitoneal space, causing a moderate amount of pain that lasted a brief time. There were no other sequelae.

The intrapleural injection occurred only once. This, again, was early in the series, when we were a little unsure of ourselves. The patient was not the one who had pleuritis following the examination.

Our main problem recently has been the subcapsular extravasation of the acetrizoate. We have been trying to correlate the splenic pulp pressure with the portal pressure. The necessity of leaving the needle in a little longer, and the rocking of the needle with respiration, has contributed somewhat to this. The needle apparently is loosened within the spleen. Injection of the dye extravasates in a retrograde fashion and outlines the splenic capsule.

We have had three failures due to nontransit that we have been unable to explain. We have injected the dye into the spleen, and it has not been picked up in the circulation.

Inevitably there will be some failure of the x-ray equipment, and this has been particularly so with the serial x-ray device we use.

There is only one other point I should like to bring out, and that is that routinely we prepare these patients just as we would for an operation.

We discuss the situation with them and tell them that there is a slight chance that hemorrhage might occur, necessitating a splenectomy. Fortunately, to date we have not had to carry out such a procedure.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: Do you have any feeling about the prothrombin level? Does that influence you when you do this examination?

DR. WILLIAM J. FRY, Ann Arbor, Mich.: We routinely check the prothrombin time, and recently we have been using vitamin K injections even though the prothrombin time is normal. We also check the platelets and any other bleeding manifestations the patient might have.

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: If the prothrombin time was 40 to 50 or below, would you still do the test?

DR. WILLIAM J. FRY, Ann Arbor, Mich.: Not until we primed the patient with vitamin K. We would not do it unless the prothrombin rose to a normal level.

Solubility of Cholesterol and Gallstones in Metabolic Material

CHARLES G. JOHNSTON, M.D., and FUMIO NAKAYAMA, M.D., Detroit

The solution of gallstones within the extrahepatic biliary tree has been repeatedly attempted, without generally accepted success. Organic solvents have been used to remove retained stones after choledochostomy, but this method has not been widely accepted because of lack of uniform success and because of the irritating properties of the solvent. Best [1,2] recommended flushing of the stones by increasing bile flow with dehydrocholic acid N. F. (Decholin), together with drugs to relax the sphincter, but did not intimate that by this procedure the stones became any smaller. Obviously, only small stones could be expected to respond to this treatment because of the small diameter of the duct even when the sphincter is relaxed.

Naunyn,[3] in 1892, stated that human gallstones placed in the gallbladder of the dog disappeared after a few months. This has been repeatedly corroborated,[4-12] and it seems clear that the stone disappears because of the solubility of the cholesterol of the stone in dog bile.

Large and Lutton [13] have demonstrated that not only the dog but also the pig, sheep, and goat will dissolve human stones placed in the gallbladder. Ox bile, as well as the bile of the dog, has been shown to have a solvent action on human gallstones in vitro. The solution of human gallstones by animal bile is a slow process in vivo or in vitro and requires long, continuous bathing of the stone in the bile and frequent replenishing of the bile as it becomes relatively saturated with dissolved cholesterol.

Most animal bile is not so different in constitution from human bile, and it seems reasonable to assume that with slight changes in the composition of human bile it might dissolve human stones, or that substances excreted into the bile may be administered which will readily dissolve cholesterol. An ideal solvent for gallstones in vivo ought to have the following characteristics: (1) Cholesterol must be readily soluble in it; (2) it must be possible to provide a continuous flow over the stones; (3) it must be nontoxic, and (4) it must be possible to introduce it into the biliary tree over a sufficient time and in adequate concentrations to be effective.

Such material is readily at hand. In 1905, Hammarsten [14] and, in 1908, Long and Gephart [15] found not only that there was phospholipid in bile but that it was associated with bile salt. This was not a simple mixture of these two substances, since the phospholipid was no longer soluble in ether. Johnston, Irvin, and Walton [16] presented data which suggested that the phospholipid in bile was lecithin. On standing, choline increases in the bile, indicating that the lecithin rapidly disintegrates. Later studies have added further proof that lecithin is the sole phospholipid in bile.[17-20]

Studies by Isaksson [21-25] corroborated the findings of Hammarsten that bile salt and lecithin formed a combination and suggested that this was probably not a true chemical combination but, rather, the result of micelle

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From the Department of Surgery of Wayne State University College of Medicine and the Detroit Receiving Hospital.

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formation. His studies indicated that cholesterol was more soluble in lecithin-bile salt than it was in bile salt alone. Our own studies with bile salt, lecithin, and combinations of bile salt, lecithin, and ox bile reveal that ox bile saturated with lecithin increases in cholesterol-holding capacity. When such fortified ox bile is extracted with ether and then with chloroform, the chloroform extract has a high concentration of bile salt and lecithin. When this material is added to fortified ox bile, the cholesterol-holding capacity increases markedly. This increased holding capacity is greater than might be expected from the increase in bile salts alone.

In 1939, in a study of the preparations and properties of lyophilized animal bile,[26] we determined that the bile salt from such a preparation was promptly absorbed from the intestine and almost quantitatively excreted in the bile. This study was enhanced by the fact that the pig has very little bile salt of the cholic acid series, while human and dog bile has no hyodesoxycholic acid, the common bile acid of the pig.[27,28] The use of dried pig bile in the human and the dog permitted quantitative studies of absorption and excretion of the foreign bile salt, and the use of dried ox bile served a similar advantage in the pig. It was therefore possible to determine that it was possible not only to replace lost bile salts by oral administration of lyophilized bile but also to increase the concentration well above normal levels.

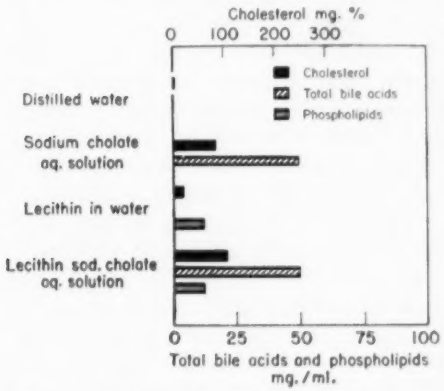

Fig. 1.—Cholesterol-holding capacity of several solutions.

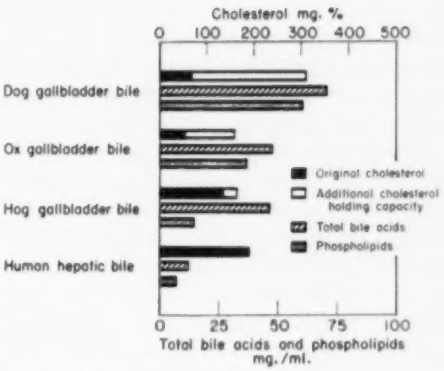

Fig. 2.—Cholesterol-holding capacity of several species.

The absorption and excretion of lecithin are also clearly demonstrated. Lecithin is normally absorbed through the thoracic duct.[29-36] The rapidity of increase of lecithin in bile after oral intake of ox bile fortified with lecithin suggests that at least some of this material may be absorbed through the portal vein.

In vitro studies indicate that the cholesterol-holding capacity of ox bile is increased by the addition of lecithin (Figs. 1, 2, and 3). If the lecithin-bile salt is extracted from lecithin-fortified ox bile and added to other fortified ox bile, the cholesterol-holding power is further increased. With the usual concentrations of bile salt maintained, the holding capacity of ox bile for cholesterol is increased about 50% by

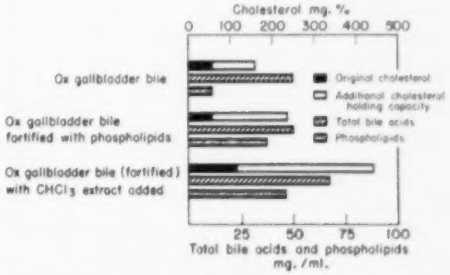

Fig. 3.—Effect of addition of phospholipids on cholesterol-holding capacity.

the addition of lecithin. With the addition of the extract to this fortified bile, the cholesterol-holding capacity is further increased well over an additional 100%. When the lecithin fortified ox bile is further fortified with the extract, the bile salt increases, but not sufficiently to account for the additional cholesterol-holding capacity.

Our studies with the solution of cholesterol in bile salt solutions suggest that there is some additional factor other than bile salt which accounts for the amount of cholesterol held in bile. Human bile is fully saturated with cholesterol. On the other hand, the bile of the dog, ox, sheep, and pig is not fully saturated with cholesterol.

Human gallstones washed with ox bile according to the procedure described by Large and Lutton [13] are slightly dissolved. When ox bile is fortified with lecithin, the stone loses weight more rapidly, and this loss of weight is further enhanced by the addition of the extract containing bile salt and lecithin (Fig. 4).

Since it is possible in the human to increase the concentrations of both bile salt and lecithin in the bile by oral intake of

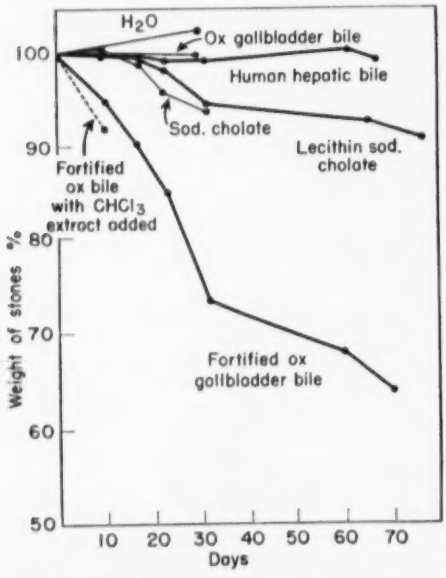

Fig. 4.—Solution of gallstones with continuous washing.

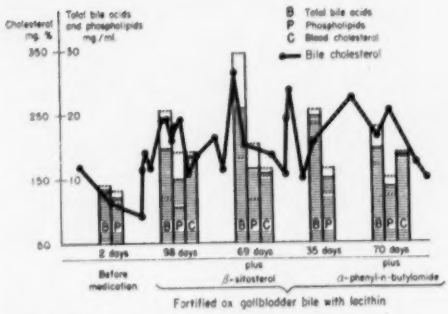

Fig. 5.—Relation of cholesterol, bile salt, and phospholipid in human bile.

lecithin-fortified ox bile, and since this material increases the cholesterol-holding capacity of bile and causes more rapid solution of gallstones in the test tube, it was felt that this material should be effective for solution of retained stones in the common duct. Accordingly, patients with common duct T-tubes in place were studied with regard to the concentrations of bile salt, lecithin, and cholesterol to determine the effect of fortified ox bile administered orally or through the T-tube. Twenty-six patients were studied, of whom five had retained stones.

As was anticipated, there was an increase of bile salt and lecithin in the bile when fortified ox bile was administered. Furthermore, high levels of bile salt and lecithin could be maintained by oral intake or by introduction of this material through the T-tube. Figure 5 illustrates this fact. It also illustrates that with increases in bile salt there is a corresponding increase in cholesterol in the shed bile. Not only does the cholesterol concentration of the bile increase, but, regardless of the concentrations of bile salt and lecithin attained in the bile, we have not been able to effect a situation where human bile as excreted increases its holding capacity for cholesterol. In other words, it is not possible to add more cholesterol to the bile than is contained therein, regardless of marked increases in bile salt and lecithin. Apparently human bile is always nearly or completely saturated with cholesterol under the conditions of our study.

We have not been able to determine whether the large quantities of cholesterol excreted in the bile in treated patients is the result of mobilization of cholesterol from existing cholesterol stores or whether the additional bile salt and/or lecithin increases the synthesis of cholesterol.

Two patients with retained common-duct stones were treated with bile salt-lecithin sufficient to maintain increased levels of these substances over a period of 9 and 13 months, respectively. Periodic cholangiograms revealed no apparent decrease in size of the stones, and in one of these patients stones were removed after 13 months of treatment. It seems obvious that, in order to dissolve stones by metabolic material such as we have used, it will be necessary to decrease the degree of saturation of cholesterol in bile. The fact that animal bile is relatively unsaturated is sufficient to account for the solution of gallstones when placed in the extrahepatic biliary tree of these animals.

In an attempt to decrease the excretion of cholesterol in the bile, we have used two substances which have been reported to decrease blood cholesterol. Sitosterol, introduced as Cytellin (20% β- and dihydro-β-sitosterols and 4% alcohol), has been reported to decrease the blood cholesterol.[37-48] It is assumed that Cytellin interferes with the absorption of cholesterol. We have introduced increasing doses of Cytellin, up to four times the recommended effective dose, with no demonstrable effect on the cholesterol concentration of the shed bile. Our patients did not have hypercholesteremia, and there was no significant consistent decrease in the blood cholesterol levels.

Likewise, α-phenyl-n-butylamide [49-55] has been reported to effect a lowering of blood cholesterol, presumably by interfering with synthesis of cholesterol. This material was also administered in the recommended maximum dosage. This likewise did not alter the concentration of cholesterol in shed bile.

Further studies are being carried out to determine the effect of other materials in which cholesterol is soluble. Chenodesoxycholic and desoxycholic acid have excellent solubility characteristics for cholesterol and also combine with lecithin. The bile we have used has cholic acid predominantly, and the addition of this material in the enterohepatic circulation causes an increase in cholesterol to saturation. In dogs there is only slight increase in cholesterol concentration in the shed bile after cholic acid administration, and these concentrations do not reach saturation levels.

It ought to be possible to introduce materials which will increase the cholesterol-holding capacity of bile as excreted without causing a concomitant increase in the excretion of cholesterol. Under such circumstances human stones ought to dissolve as readily in the human as is now evident when these are placed in the extrahepatic biliary tree of the dog.

Summary

It is possible to introduce normal metabolic materials effective for solution of gallstones into the bile of the human. Bile salt-lecithin has excellent solvent action on cholesterol and can be introduced into human bile and high levels maintained. However, with increases in bile salt-lecithin there is a corresponding increase in cholesterol concentrations in the bile.

Department of Surgery, Wayne State University College of Medicine.

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DISCUSSION

DR. ALFRED M. LARGE, Detroit: As many of you know, Dr. Johnston has been interested in the chemistry of bile and its relation to gallbladder disease for many years. Some time ago Lutton and I became concerned with one small phase of this problem, particularly as it relates to gallstones, and I should like to tell you a little about our experiences and emphasize one or two points that the authors has made.

(Slide) First we tried to confirm the work of others on solution of human gallstones in animal gallbladders, and put gallstones in the gallbladders of a number of animals. This slide shows that human gallstones disappear when placed in the dog's gallbladder. We also found that the same thing is true in the pig, the sheep, and the goat. All these animals, as you know, have bile which is rather low in cholesterol.

(Slide) We thought that if we could do this in a test tube as well as in the living animal, we might obtain some additional information. The slide shows the type of device that we used. Given a glass tube with an arm on it and fluid in it up to this level, suction is applied so that air will pass over and out to a vacuum pump. Obviously when the air bubbles come over with fluid above the level of this arm, the air bubbles will bring over a little fluid with them, and so there will be a continuous gentle passage of fluid over this platform, on which may be placed gallstones.

(Slide) To summarize some of our observations using this apparatus, if dog hepatic bile is used from common-duct fistulae, the human stone in this apparatus will lose 1.03 mg. of weight each day; with dog gallbladder bile it will lose 4.28 mg., and with human hepatic bile it loses 0.09 mg. With dog hepatic bile mixed with cholesterol until it is saturated, the stones no longer dissolve.

This shows, as many have thought for a long time, that it is the cholesterol that is important in this dissolution.

Dr. Johnston and Dr. Nakayama have shown that if you use lecithin as well as bile salts in human bile you may increase the cholesterol-hold-

ing power of that bile, and therefore you might be able to dissolve human gallstones. This is easy enough to do in a test tube, and their experiments have proved it very nicely. The trick is to get it to work in living patients who have stones. The authors have shown that one can raise the lecithin, which I think is important, and the bile salt concentration in bile in humans; but at the same time, curiously enough, the cholesterol concentration of the bile also goes up. If this could be done without increasing the cholesterol concentration of the bile, we would have something; we would really be in business!

DR. CHARLES G. JOHNSTON, Detroit: The problem of the retained stone is a serious one. The matter of operating to remove the stones gives us a great deal of trouble. If we had some means of removing the stones by metabolic means, it would be excellent.

Dr. Nakayama has demonstrated the fact that all of the postulates necessary for solution of stone have already been established. However, when one gives this material to patients, a rather strange thing happens; a great deal more cholesterol is poured out with the increase in concentrations of lecithin and bile salt.

The bile salt we employed was predominantly cholic acid, using extracts of ox bile. This material does cause a great response in relation to the increase in cholesterol in shed bile, not only in humans but also in animals. In other words, the bile is always saturated, even if the amount of material which would dissolve cholesterol is increased.

Whether or not there are other substances, we do not know for certain; but we have some hope from preliminary studies that there are other substances which will not cause this great increase in cholesterol excretion to saturation.

We have an easy way to study this. We can study whether or not the bile is saturated, and therefore we can tell whether cholesterol will be dissolved from the stone. This is an ideal set-up for dissolving stones. In the test tube this is a very poor method of dissolving gallstones because there is one mass of solution and when that becomes saturated no more washing will cause a decrease, whereas in the human the stone can be constantly washed in fresh bile. Therefore the dissolution of stones by metabolic material should be an ideal method.

We are now studying some of the bile acids, such as desoxycholic and chenodesoxycholic, which are found in human bile in smaller quantities. They are a little hard to come by in pure solution; so we have had to synthesize them ourselves in order to use them. It may well be that some of the other bile acids—and, by the way, these other bile acids that I spoke about have a higher solubilizing effect on cholesterol—do not increase the excretion of cholesterol along with their increase in human bile; then there should be little doubt that the stone will be dissolved.

We are reporting an unsuccessful experiment, obviously, even though we have all the postulates covered but one; but we are heartened by the fact that it should now be purely a matter of trying one substance after another until we find one which will not increase cholesterol and cause saturation of human bile. That ought to be possible, because in animals this is a common situation, for animal bile is unsaturated.

Recognition and Treatment of Congenital Choledochal Cysts

WILLIAM J. GROVE, M.D., Chicago

Congenital cystic dilatation of the common bile duct is an uncommon lesion but one which may be recognized clinically. The diagnosis may be made preoperatively with relative ease if the possibility is considered, since the symptoms and findings are usually fairly clear-cut. The rarity of the lesion is indicated by a calculation from published data.[1,5,8] It would appear that a congenital choledochal cyst will be found approximately once in 200,000 general hospital admissions. The five cases being reported indicate an incidence of 6 per 100,000 general hospital admissions. Approximately 250 cases have been reported to date. It is the purpose of this paper to present five cases of congenital choledochal cyst and to discuss diagnostic procedures, as well as various methods of therapy.

The etiology and pathology of this unusual lesion have been adequately discussed in many reviews of the subject.[3,7] It need only be pointed out that the lesion is probably of congenital origin, resulting from some defect in the formation of the common bile duct. The wall of the cyst is composed of fibrous tissue and is unlined. The absence of a lining in the cyst may be of importance in suggesting the cause for failure of surgical correction in some instances.

Signs and Symptoms

Choledochal cysts are four times as common in females as in males. When the symptoms of jaundice, pain, and sometimes fever and vomiting are present in a girl in whom a mass is palpable in the right upper quadrant, the diagnosis of choledochal cyst must be entertained. The symptoms described frequently occur in attacks, with remissions of many months. Jaundice was present in about two-thirds of the cases reviewed in the literature. It was present in three of the five cases to be reported. A palpable tumor is usually present, although cases have been reported in which biliary symptoms were present with a cyst too small to be detected clinically. Pain is nearly always present to some degree. Vomiting presumably occurs when the cyst is large enough to compress the duodenum. Fever is presumed to be due to infection of the cyst contents, with ascending cholangitis. An analysis of the incidence of various symptoms of cases reported in the literature has been made by Shallow[2,6] and others. The disease may be confused with pancreatic cysts, retroperitoneal tumors, and primary liver disease. About 50% of cases have been diagnosed before the age of 14 years. One case was reported in a patient beyond 70 years of age.

Laboratory Findings

Ordinarily the routine blood examination and urinalysis are normal except for evidences of jaundice, if it is present. Liver function tests will commonly demonstrate the signs of obstructive jaundice. The jaundice may be unrelenting, but ordinarily is fluctuating, with alternating cholic and acholic stools. The serum amylase may be elevated, suggesting an obstruction to the normal flow of pancreatic juice. X-ray examination of the upper gastrointestinal tract may show displacement of the duo-

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Fig. 1 (Case 4).—Upper gastrointestinal tract x-ray study, showing compression of duodenum by extensive mass.

denum or stomach by the mass in a rather typical fashion (Fig. 1).

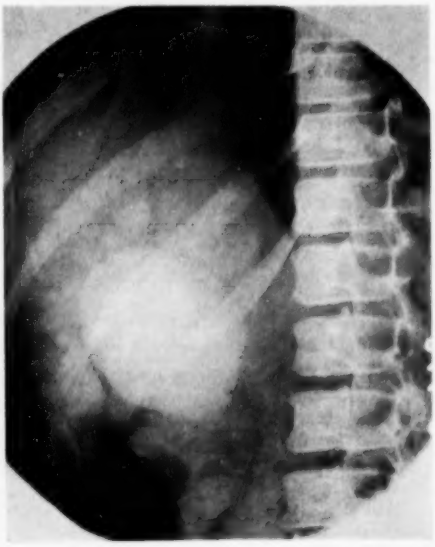
When the patient with a choledochal cyst is not jaundiced, a nearly absolute diagnosis may be established by an intravenous cholangiogram (Fig. 2). Since such a patient usually has periods when he is free of jaundice, it may be wise to delay surgery, especially in a child with undiagnosed jaundice, for a short period to see whether the jaundice clears. A cholangiogram may then be obtained. Occasionally the oral administration of gallbladder dye will visualize a cyst of the common duct.

Case Material

Five female patients, on whom the diagnosis of congenital choledochal cyst was made, have been seen at Research and Educational Hospitals within the past 10 years. These are the only known cases in clinical and autopsy material in approximately 80,000 hospital admissions over a 10-year period. All of the patients have survived surgery and are now living. In all five patients the diagnosis was suspected preoperatively, and in one the diagnosis was absolutely established by intravenous cholangiography. The method of treatment has varied and will be indicated in each case. The Table summarizes the data on each patient.

Case 1.—A 36-year-old white woman was admitted to Research and Educational Hospitals in February, 1946. Since the age of 10 years she had noted frequent bouts of nausea and vomiting, as often as five or six times per week. To her knowledge, she had never been jaundiced and had not had clay-colored stools or dark urine. During the year prior to admission she had noted frequent bouts of shaking chills and fever with moderately severe right upper quadrant pain. For the month prior to admission she had noted a fullness in the right upper quadrant. The physical examination was essentially negative except for a mass distinct from the liver, but just beneath it, in the right upper quadrant. All laboratory findings were normal, including liver function tests. The x-ray studies of the upper gastrointestinal tract revealed a displacement of the duodenal loop and was interpreted as diagnostic of a pancreatic or choledochal cyst (Fig. 3). On Feb. 15, 1946, the patient was operated upon and a choledochal cyst was found. A loop of jejunum was anastomosed to the cyst, which contained approximately 1 pint (500 cc.) of bile. An enteroenterostomy was made between the proximal and distal loops of the jejunal loop. Recovery was uneventful, and the

Fig. 2 (Case 4).—Intravenous cholangiogram, which outlines cyst, as well as intrahepatic ducts and a compressed gallbladder.



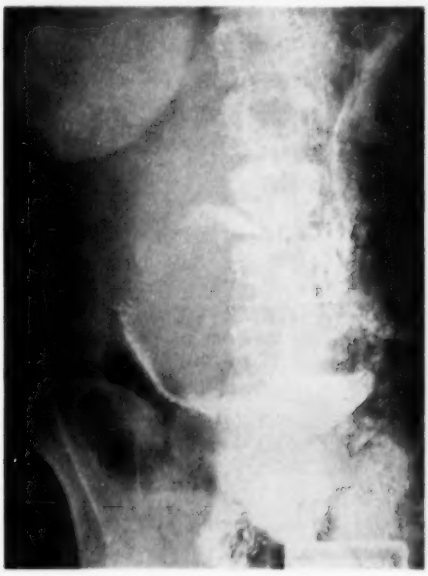
Summary of Cases

Case	Age	Symptoms	Findings	Treatment	Follow-Up
1	36 yr.	R.U.Q. pain	R.U.Q. mass	1. Choledochocystojejunostomy (loop type)	10 yr.; asymptomatic
2	8 yr	R.U.Q. pain; vomiting; jaundice; fever	R.U.Q. mass	1. Choledochocystoduodenostomy 2. Choledochocystojejunostomy (loop type)	10 yr.; unsatisfactory
3	7 mo.	Jaundice	R.U.Q. mass	1. Choledochocystojejunostomy (loop type) 2. Cholecystojejunostomy (Roux-en-Y type)	8 yr.
4	9 yr.	Fever; vomiting	R.U.Q. mass; high amylase; cyst demonstrated cholangiographically	1. Choledochocystojejunostomy (Roux-en-Y type)	1 yr.; asymptomatic
5	12 yr.	Jaundice; fever	R.U.Q. mass	1. Choledochocystojejunostomy (Roux-en-Y type)	8 mo. asymptomatic

patient has remained asymptomatic for the past 10 years.

Comment.—There was no question as to the diagnosis in this case at surgery, since the hepatic ducts were noted to enter the cyst. A duct was noted leaving the cyst in the direction of the duodenum, although a probe could not be passed into the duodenum. However, since the patient was not jaundiced, there must have been some degree of patency. This case illustrates the fact that, except for the vomiting, a cyst may be present for many years without causing biliary tract symptoms.

Fig. 3 (Case 1).—Upper gastrointestinal tract x-ray study, showing marked distortion of the duodenum by extensive mass.



Case 2.—An 8-year-old Mexican girl was first admitted to Research and Educational Hospitals in 1947. Since the age of 9 months she had had recurrent attacks of jaundice with light stools and dark urine, vomiting, and right upper quadrant pain. In 1945 an appendectomy had been done during an attack of vomiting, pain, and fever, without jaundice. In 1946 the true situation was recognized, and in another hospital the cystic dilatation of the common duct had been anastomosed to the duodenum. Although the patient had been symptom-free for a short time after this operation, the symptoms had returned. On Oct. 1, 1947, an exploration was again done. The previous choledochocystoduodenostomy was completely closed. A loop of jejunum was anastomosed to the cyst with a proximal enteroenterostomy, as in the previous case. The patient has remained relatively asymptomatic, until recent months. Rather severe bouts of chills and fever and intermittent jaundice have developed. Upper gastrointestinal tract x-ray studies reveal reflux of barium into the biliary tract. Intravenous cholangiography now reveals dilatation of the intrahepatic biliary ducts. However, liver function, as measured by thymol turbidity, cephalin flocculation, and alkaline phosphatase, is normal. It is probable that a re-exploration should be done in order to see whether the choledochocystojejunostomy has become stenotic. If stenosis is not present, the proximal arm of the jejunal loop must be divided so that food will not pass the stoma.

Comment.—This case demonstrates that anastomosis between the cyst and the gastrointestinal tract may close. It also demonstrates that it is probably unwise to attach a jejunal loop to the biliary tract without providing a by-pass for food, e. g. a Roux-en-Y arm, since it has been demonstrated that there is reflux of food into the biliary tract. The patient, now 18 years old, is mentally retarded, and evaluation of her symptoms is difficult.

CASE 3.—A 7-month-old female infant was first seen at Research and Educational Hospitals in 1949. The child had had a replacement transfusion at birth because of severe jaundice. At the age of 4 or 5 months a mass was noted in the right upper quadrant. By this time the jaundice had completely cleared. Although the diagnosis of choledochal cyst was entertained, the final diagnosis was not made until surgery, on March 25, 1949. At that time a jejunal loop with a proximal enteroenterostomy was anastomosed to the cyst. Recovery from surgery was uneventful, and the child was asymptomatic for approximately two years, when recurrent attacks of chills, fever, jaundice, and acholic stools appeared. A reexploration was done on March 28, 1951. At that time it was noted that the cyst had completely regressed and that there was no stoma between the cyst and the jejunal loop. The common duct seemed very narrow and scarred, and the gallbladder was markedly distended. Therefore, the jejunal loop was separated from the cyst, converted to a Roux-en-Y arm, and a cholecystojejunostomy performed. Recovery from this surgery was excellent. The child was rehospitalized again in 1952 because of an attack of what was presumed to be cholangitis. Since that time she has remained entirely well. Her father is a physician and reports no evidence of obstruction or ascending cholangitis. At this time the liver function tests are all normal. The child has developed normally.

Comment.—Stenosis of the anastomosis between the cyst and the gastrointestinal tract occurred again in this case. Regression of the cyst, and even stenosis of the duct, occurred. Apparently after the cholecystojejunostomy (Roux-en-Y type) adequate drainage was established.

CASE 4.—A 9-year-old white girl was first seen at Research and Educational Hospitals in March, 1956. The history revealed that she had had nausea and vomiting, right upper quadrant pain, and intermittent fever for one and a half years. The mother thought that at times there may have been slight jaundice. The patient had been explored approximately one year prior to admission for appendicitis. At that time a cyst in the area of the gallbladder was found. The physical examination was negative except for a palpable mass in the right upper quadrant. Laboratory studies were negative except for serum amylase levels, which ranged in the neighborhood of 500 units, even when the patient was asymptomatic. Since the patient was not jaundiced, an intravenous cholangiogram was done, which revealed a cyst of the common duct (Fig. 2). At surgery a Roux-en-Y arm of the jejunum was constructed, and an anastomosis made between the Roux-en-Y arm and the cyst. The patient has remained symptom-free for one year. Postoperative intravenous cholangiogram revealed a shrunken cyst, without evidence of obstruction.

Comment.—This case demonstrates the validity of intravenous cholangiography as a diagnostic measure and its value in estimating the postoperative course of the patient. Further, this case represents one in which jaundice was not a prominent symptom.

CASE 5.—A 12-year-old white girl was admitted to Research and Educational Hospitals in July, 1956, complaining of jaundice for six weeks. On admission there was a tender mass in the right upper quadrant. The mass initially was indistinguishable from the liver, but subsequently could be well defined as separate from the liver. A needle biopsy of the liver was done and interpreted as showing cholangiolitic hepatitis. The patient was placed on large doses of cortisone. Barium studies of the upper gastrointestinal tract revealed marked displacement of the duodenum (Fig. 4). When the mass in the right upper quadrant became distinguishable from the liver, a diagnosis of choledochal cyst was made and surgery undertaken, in July, 1956. A large cyst, which contained approximately 800 cc. of bile, was found (Fig. 5). A Roux-en-Y arm was constructed and anastomosed to the cyst. Liver biopsy at this time revealed mild to moderate biliary cirrhosis. The

Fig. 4 (Case 5).—Upper gastrointestinal tract x-ray study, revealing displacement of duodenum by extensive mass.

Fig. 5 (Case 5).—Photograph taken during operation on a choledochal cyst, which contained 800 cc. of bile. The cyst displaced the liver upward and the transverse colon downward.

patient's postoperative course was uneventful. On Dec. 6, 1956, the bilirubin was normal, and all of the liver function tests were essentially normal except for a serum cholesterol level of 700 mg. per 100 cc.

Comment.—This patient represents a case in which the diagnosis could not be made by the use of intravenous cholangiography because of the presence of jaundice. A postoperative cholangiogram (Fig. 6) carried out through a catheter left in place during surgery revealed some retention in the cyst.

Fig. 6.—Postoperative cholangiogram showing filling of cyst with drainage via Roux-en-Y anastomosis. The cyst did not drain completely unless patient was erect.

General Comment

Although the older patient (Case 1), who was treated by choledochocystojejunostomy (loop type), has remained asymptomatic, no studies have been done to demonstrate reflux of intestinal contents into the biliary tree. The second patient, in whom a similar procedure was done, has had recurrent bouts of ascending cholangitis and laboratory evidence of reflux into the biliary tract. It appears that further surgery will be necessary in this case. It is believed that reflux with resulting cholangitis will occur frequently with this type of operation. Hence, such a procedure is not recommended.

In the infant, in whom the jejunum was anastomosed directly to the cyst, the anastomosis became stenotic within a relatively short period and appeared to have produced narrowing of the duct, so that the gallbladder remained distended. Anastomosis of a Roux-en-Y arm to the gallbladder has been entirely satisfactory. The absence of a lining in the cyst precludes the possibility of a direct mucosa-to-mucosa anastomosis. It is probable that all such anastomoses will tend to close. Long-term follow-up of all

patients with choledochocystoenterostomies will prove this point.

The advocates of direct anastomosis of the cyst to the duodenum use as their argument for such a procedure the fact that complete diversion of the bile from the duodenum, as with a Roux-en-Y anastomosis, promotes a situation which will allow the development of duodenal ulceration. None of the present patients have known ulcer symptoms. Four of the five patients have had repeated upper gastrointestinal tract x-ray studies to determine, if possible, the presence of such ulcers. None have been found. Duodenal ulcer development has not been a problem in a much larger group of patients who have had the Roux-en-Y type of common bile duct reconstructions. On the other hand, a Roux-en-Y arm or jejunal loop with an enteroenterostomy tends to prevent the regurgitation of food into the biliary tract and should reduce the incidence of ascending cholangitis. Keeley [4] is credited with first recommending a Roux-en-Y type of anastomosis for drainage of a choledochal cyst.

The importance of establishing a diagnosis preoperatively has been pointed out by Tsardakas and Robnett.[5] In an analysis of 57 of the most recently reported cases in the literature, they found that if the diagnosis was suspected preoperatively, the mortality was 21.4%. If no diagnosis was made preoperatively, the mortality was 31.6%. Intravenous cholangiography will give good visualization of the cyst if jaundice is not present. It is believed that this method of evaluation will greatly increase the possibility of preoperative evaluation, since at least one-third of the patients are not jaundiced and the remainder may have remission of jaundice. The biliary cirrhosis which was present in the last patient suggests that the earlier the diagnosis can be made, and adequate drainage established, the better the possibility of long-term survival. Furthermore, intravenous cholangiography may be used to demonstrate postoperative results.

Excision of the entire cyst with anastomosis of the proximal duct to the gastrointestinal tract has been recommended by many in the literature. This seems unwise from several points of view. Tedious dissection of the cyst can become hazardous and undoubtedly would increase the operative mortality. Second, any anastomosis between the biliary tract and the gastrointestinal tract is apt to result in difficulties in the long run. When the cyst, and possibly the gallbladder, have been excised initially, great difficulty may be found in trying to establish adequate drainage, should further surgery be needed. The second case demonstrates the value of the gallbladder having been left undisturbed for possible future use.

It is worth noting that in all the cases presented a misdiagnosis had been made at least once before the proper diagnosis was made, thus emphasizing the necessity of considering choledochal cysts as a possible diagnosis, particularly in female children.

Most authors have indicated that choledochal cysts are unlined by epithelium. In none of the five cases presented could an epithelial lining be demonstrated. The absence of a lining precludes a mucosa-to-mucosa anastomosis. The lack of epithelium in the cyst may explain the failure of some anastomoses to remain patent for long periods.

Summary

Five patients with congenital choledochal cyst are presented, three of whom have been followed seven years or longer. Two of these patients have done well; one has had two operations on the biliary tract and probably will require further surgery. Two recent patients are now symptom-free, but will require many more years of follow-up before final evaluation can be made.

Intravenous cholangiography has been demonstrated to be of value in the diagnosis of congenital choledochal cysts.

A Roux-en-Y type of choledochocystojejunostomy is recommended as the pro-

cedure of choice in the treatment of choledochal cysts.

Department of Surgery, University of Illinois College of Medicine.

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Extensive bibliographies may be found in References 5 and 8.

DISCUSSION

Dr. John L. Keeley, Chicago: This paper is very interesting, and I congratulate Dr. Grove on the management of this rather long series of unusual cases. I believe there may be 200 or 250 cases of this lesion reported. To have five such cases represents a large series.

As Dr. Grove said, the triad of pain, jaundice, and a right upper quadrant mass certainly is not present in all cases. With the advent of intravenous cholangiography, it will be possible, I am sure, to make a preoperative diagnosis in many of these cases in which it had not been possible to do so before. If the preoperative diagnosis is not made, certainly the awareness of the possibility of such a lesion forewarns the surgeon should he encounter something unusual in the right upper quadrant.

In 1946 we encountered such a lesion; I have two slides to show what we did with the lesion.

(Slide) This was a 30-year-old man who had never been in good health. He had been regarded as a sickly child by his family. Various diagnoses, including anemia and a number of other vague disturbances, had been made. Finally he was studied more completely and found to have no visualization of the gallbladder by the oral method; so the abdomen was explored. There had been jaundice and pain, but no mass. The findings appear in the illustration on the left. We thought it would be better to open this cyst to find out exactly what it was. As you see here, we were able to probe the common duct. We constructed a Roux-en-Y anastomosis, which seemed to be the best solution at the time; and perhaps Dr. Grove's series may indicate that it was a wise choice.

We felt as Dr. Grove did, however, that to preserve the gallbladder might give us something further to work with if the Roux-en-Y did not function properly. We were somewhat concerned about making this anastomosis, because these cysts, whether from distention, with ischemia of the wall, or something else, are certainly parchment-thin, many of them, and they make poor material to use for an anastomosis.

(Slide) This shows the mechanism by which intermittent jaundice occurs in these patients. When the ball valve is closed here, and the cyst partially filled, the patient becomes jaundiced. When the cyst becomes large enough, if the opening down here is arranged properly, it will open and drain, the attack will subside, and the patient will recover.

Studies taken then usually do not show much if any abnormality. In the absence of the availability of intravenous cholangiography, it is not hard to understand how these cysts can be missed.

This 30-year-old patient, who had had symptoms practically all his life, is one of the few reported patients in whom stones have accumulated in the cyst. They are shown here. We have no information about the nature of these stones. They were not examined further. It is unusual, I believe, to find stones in a cyst of this kind.

When Dr. Grove told me about his paper and asked me to discuss it, a few days ago, I called this patient and found that after 11 years his Roux-Y anastomosis is functioning properly. He has had no ascending cholangitis and has done very well.

It would be interesting to call back these patients, such as Dr. Grove's case of long-term follow-up of 10 years, now that we have intravenous cholangiography, and see what happens to the cyst. The one Dr. Grove showed certainly was shrunken. I wonder whether the cyst shrinks down to make a satisfactory channel or whether it still becomes dilated at intervals.

Sclerosing Carcinoma of the Major Intrahepatic Bile Ducts

WILLIAM A. ALTEMEIER, M.D.; EDWARD A. GALL, M.D.; MAX M. ZINNINGER, M.D., and PAUL I. HOXWORTH, M.D., Cincinnati

Primary carcinoma of the bile ducts may be extrahepatic or intrahepatic in origin. The clinical and diagnostic features of the more prevalent extrahepatic forms are well known, but considerably less information is available for the intrahepatic variety.[1-5] Carcinomas arising from the mucosal cells of the finer radicles of the intrahepatic biliary tree are known as cholangiomas and are usually considered to be an uncommon form of primary neoplasm of the liver.[6] There is another unusual type of primary carcinoma of the intrahepatic ducts which is rarer and more difficult to recognize. This form arises from the major intrahepatic ducts near the hilus. Its insidious nature, the ease with which it mimics other biliary tract disorders, and its relative inaccessibility to surgical approach are factors which have made diagnosis very difficult, and frequently impossible until autopsy.[2-4]

Since 1950, three patients with primary adenocarcinoma of the intrahepatic bile ducts have been seen on the surgical service of the University of Cincinnati College of Medicine. These cases illustrate the above features and other noteworthy characteristics, including surprisingly long survival times and repeated difficulties encountered in the establishment of a diagnosis from biopsies. Both these features were suggestive of benign obliterative cholangitis rather than malignant disease. Of incidental interest has been the opportunity provided in one case to follow the development of obstructive biliary cirrhosis by serial biopsies of the liver over a three-year period.

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From the Department of Surgery (Drs. Altemeier, Zinninger, and Hoxworth) and the Department of Pathology (Dr. Gall), University of Cincinnati College of Medicine, and the Cincinnati General Hospital.

Report of Cases

CASE 1.—A 32-year-old white man was first hospitalized in July, 1950, because of upper abdominal pain, nausea, vomiting, and jaundice. Cholecystectomy was performed, but the symptoms persisted. In November, 1950, abdominal exploration showed moderate dilatation of the common duct and apparent narrowing of the ampulla of Vater. Duodenotomy and pyloroplasty were performed, and a T-tube was inserted into the common duct. The tube was removed at the end of two weeks.

Shortly after discharge all symptoms reappeared, and he then came under our observation for the first time. A transcutaneous needle biopsy of the liver revealed "obstructive jaundice" (Fig. 2A), and in February, 1951, another laparotomy was performed, revealing the common duct to be narrowed (Fig. 3). The duct was found to terminate at the hilus of the liver, and a series of transverse sections made in the edematous and fibrous tissue in this region revealed neither the major bile duct nor a flow of bile. Microscopic examination of a hilar biopsy specimen showed dense collagen tissue, in which were embedded several acinar structures resembling bile ductules. Because of the excellent degree of differentiation, the process was interpreted then as non-neoplastic ductular residua from a cicatrized hepatic duct (Figs. 1A and 1B). A Roux-Y was developed and the defunctionalized loop of the jejunum was sutured to the hilus in the hope of providing egress of bile. Postoperatively, the jaundice diminished and bile reappeared in the stools. At this time the presumptive diagnosis was sclerosing cholangitis.

The improvement was transitory, however, and during succeeding months all of the symptoms returned. A Longmire hepatojejunostomy was done in January, 1952, after excising a triangular wedge of hepatic substance from the left lobe. Microscopic examination of hilar tissue removed at this time revealed dense scar tissue, containing groups

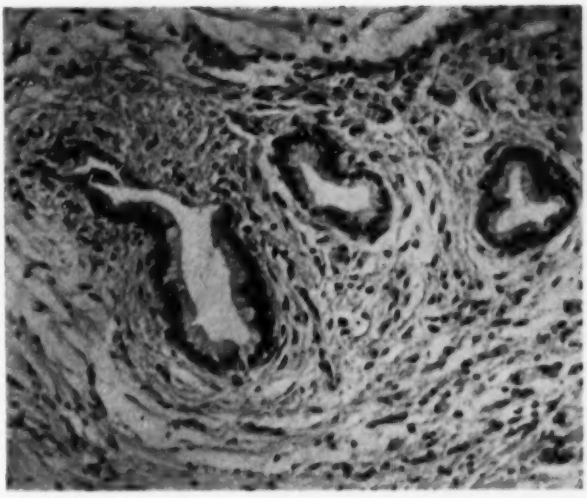

Fig. 1A (Case 1).—Surgical biopsy specimen procured from the hilus of the liver in 1951. Neoplastic acini are well differentiated and simulate those seen in bile ducts scarred by non-neoplastic inflammatory conditions.

of foam cells but no epithelial structures, neoplastic or otherwise. The liver substance removed was the seat of severe bile stasis and angioma-like bile-duct proliferation in the enlarged portal areas. There was no decrease in the jaundice at this time, and the patient was discharged in April, 1952.

With development of chills, fever, and pleural effusion, the patient was readmitted in July, 1952. Bilateral thoracotomy was carried out and drainage tubes inserted. In February, 1953, another laparotomy was carried out, in a futile effort to find and anastomose a fistulous biliary tract to the intestine. Additional tissue excised from the right hepatic lobe revealed progression of the portal area lesion with persistence of the pseudoangiomatous ductule proliferation and increased fibrosis. The pattern was that of severe, progressive biliary cirrhosis.

The patient's final admission was necessitated in November, 1953, for persistent vomiting and intense jaundice, even though two biliary fistulae developed. A seventh laparotomy was performed after roentgen studies showed obstruction of the third portion of the duodenum. At this time the omentum was studded with nodules of metastatic neoplasm, which proved to be adenocarcinoma. Although relieved of the duodenal obstruction, the patient remained deeply jaundiced and gravely ill. He died Jan. 12, 1954, three and one-half years after his first operation.

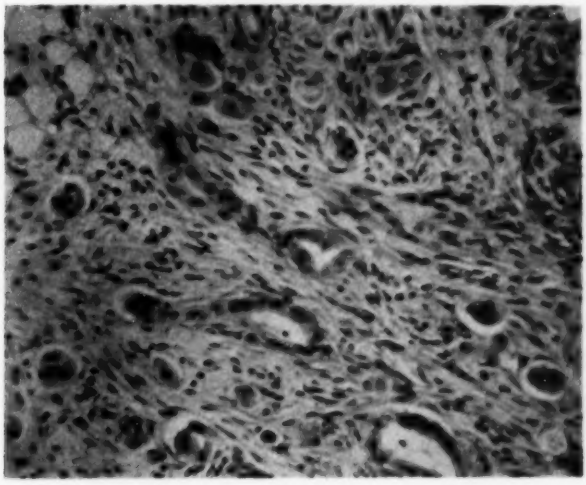

Fig. 1B (Case 1).—Another area in the same specimen illustrated in Figure 1A. Here, many of the epithelial components fail to form acini. The lesion is recognizable as scirrhous carcinoma.

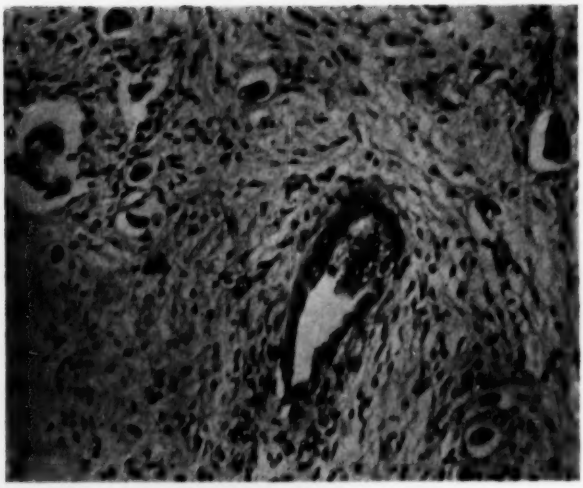

Fig. 1C (Case 1).—Surgical biopsy specimen of omentum obtained in 1954, revealing metastatic adenocarcinoma.

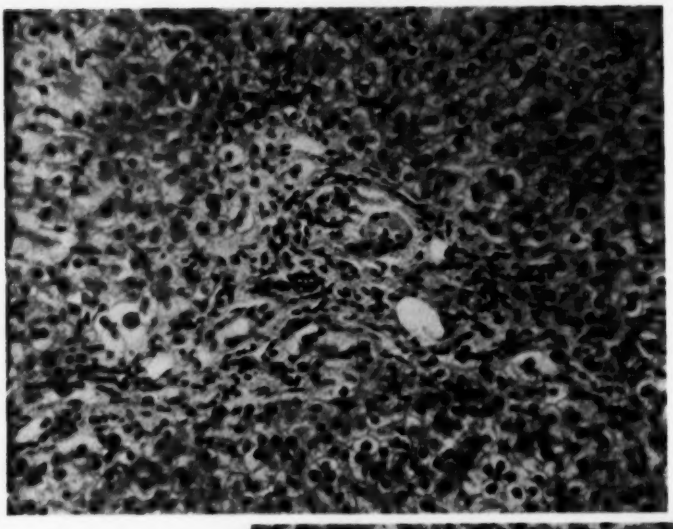

Fig. 2A (Case 1).—Needle biopsy specimen of the liver procured in January, 1951, demonstrating portal area inflammation, early bile duct reduplication, and cholangitis. Liver cells are intact. Centrilobular bile stasis, a prominent feature, is not shown in the photograph.

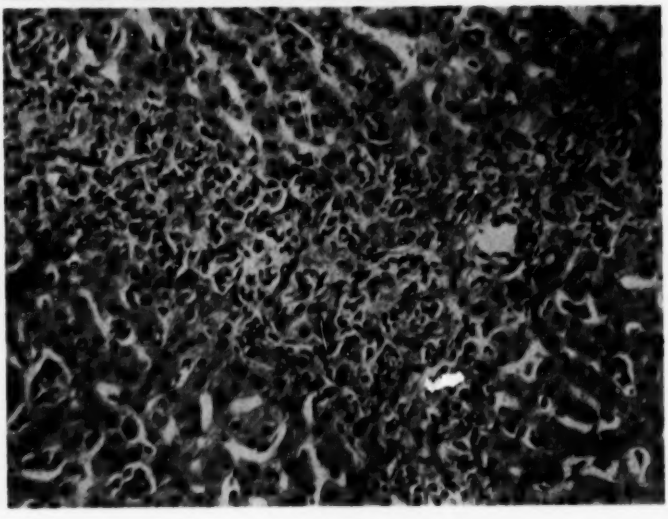

Fig. 2B (Case 1).—Liver biopsy specimen in March, 1951, depicting significant enlargement of the portal area and striking ductal proliferation. Accompanying this is a heavy neutrophil exudate.

Fig. 3 (Case 1).—Operative cholangiogram made in February, 1951, revealing a narrowing of the common bile duct and obstruction at the junction of two hepatic ducts.

At necropsy, a hepatopleural fistula was noted to have been drained through the thoracotomy wound in the right chest. The intrahepatic terminus of the tract proved to be a series of intercommunicating and loculated hepatic abscesses, which measured 2 to 8 cm. and which honeycombed the superior substance of the enlarged right lobe of the liver to a depth of 6 cm. The peritoneum was studded with innumerable plaques of metastatic carcinoma. The head of the pancreas was firmly adherent to the undersurface of the liver, and its body and tail were fibrotic and atrophic.

The liver substance was leathery and dark green and contained multiple minute abscesses, in addition to the larger ones described above. Reexamination of earlier sections as far back as February, 1951, indicated that the lesion was and had been a well-differentiated adenocarcinoma of the biliary ducts.

The final necropsy diagnoses were as follows:

(1) adenocarcinoma arising in a hepatic bile duct, with extension to the pancreas and metastases to the peritoneum and regional lymph nodes; (2) cholangitic abscesses, multiple; (3) hepatopleural cutaneous fistula; (4) obstructive biliary cirrhosis, severe; (5) esophageal varices; (6) hepatojejunostomy and duodenojejunostomy; (7) pulmonary embolism, septic, multiple; (8) acute fibrinous pericarditis.

Case 2.—A 43-year-old white man developed jaundice in May, 1950. Two months later, abdominal exploration by another surgeon revealed an area of stenosis high in the intrahepatic portion of the left hepatic duct. The duct was dilated from below, and a cytological smear was made from material curetted from it. The postoperative course was complicated by spontaneous perforation of a chronic duodenal ulcer, severe gastrointestinal hemorrhage, and later wound dehiscence, requiring secondary closure. Improvement ensued; the jaundice cleared, and the patient was discharged. The material recovered from the common duct was reported as "probable adenocarcinoma," but later consultation with several pathologists left this diagnosis in doubt. The specimen is not available for current review.

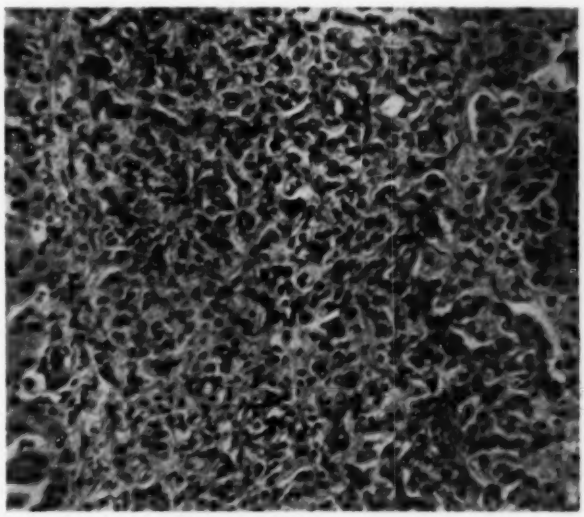

Fig. 4A (Case 1).—Liver biopsy specimen in 1952, which highlights a severe degree of ductular proliferation with capillary angioma-like appearance of the portal area. The exudate persists, and there is increased fibrosis.

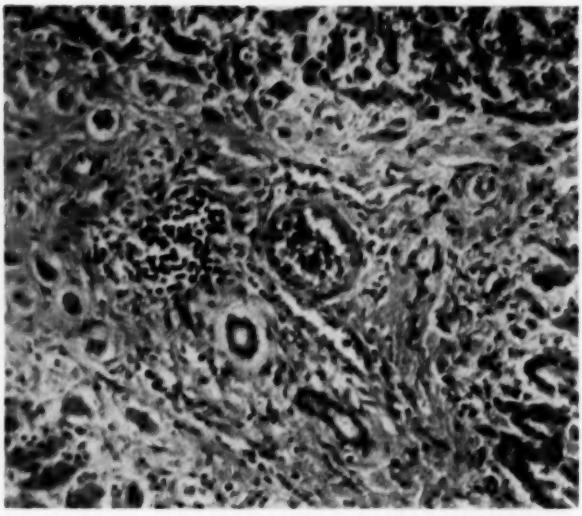

Fig. 4B (Case 1).—The liver at necropsy in 1954. The portal area is cicatrized, and evidence of significant bile-duct proliferation is lacking. A few ductules remain in the perilobular scar.

In May, 1951, the patient first came under our observation after recurrence of jaundice accompanied by fever, vomiting, and epigastric pain. The abdomen was reexplored and dense scarring found in the hilus of the liver and about the gallbladder in relation to a penetrating duodenal ulcer. Biopsy of this scar revealed no neoplasm (Fig. 5A). Again, the biliary system was probed, the stricture of the left hepatic duct was dilated, and a T-tube was reinserted into the common and hepatic ducts. A subtotal gastric resection was also carried out for the chronic penetrating duodenal ulcer. His postoperative response was excellent, and the jaundice subsided.

During the next two years there were no major complaints, but in May, 1953, jaundice reappeared and operation again became necessary. It was not possible to dilate the occluded left hepatic duct, and a T-tube was reinserted. Postoperative cholangiograms demonstrated excellent filling of the intrahepatic biliary radicles in the right lobe, but negligible traces of the opaque medium appeared in the left (Fig. 6A).

A year later (May, 1954), because of continued jaundice and intense pruritus, the patient requested reexploration. The common duct was located with difficulty, due to considerable scarring and distortion, and efforts to dilate the left hepatic duct

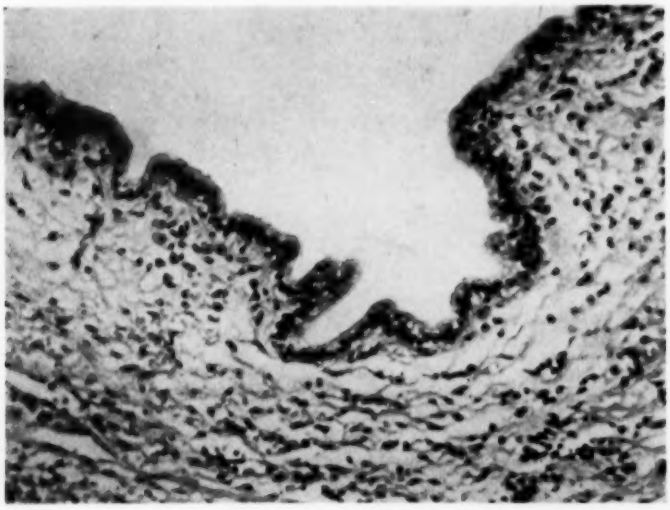

Fig. 5A (Case 2).—Biopsy specimen of granuloma of the hilus of the liver procured in May, 1951. A dilated, but empty, bile duct courses through inflamed connective tissue.

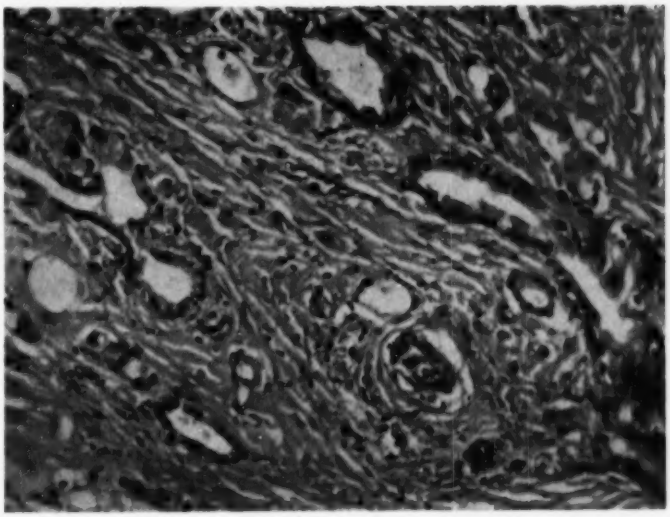

Fig. 5B (Case 2).—Section of the main left hepatic duct at necropsy in November, 1955, revealing the lesion to be a scirrhous adenocarcinoma with malformed but well-differentiated neoplastic acini embedded in a dense collagenous stroma.

were again unsuccessful. There also appeared to be some narrowing of the right duct. A T-tube was replaced, and a cholangiogram was made (Fig. 6B). With the postoperative administration of antibiotic agents, some reduction of icterus occurred.

Several times during the next year, medication with oxytetracycline (Terramycin) and chloramphenicol (Chloromycetin) appeared to be of some benefit, particularly in controlling episodes of high fever. The patient's final admission occurred in July, 1955. In a desperate effort to provide relief from the pruritus, a fifth laparotomy was performed in October, 1955. A mass, measuring 3 by 5 cm. and involving the anterior surface of the right lobe of the liver, was observed and biopsy specimens taken (Fig. 6C). No neoplasm was reported in these specimens. A hepatojejunostomy was considered but not done because of the operator's opinion that the lesion was carcinoma. Postoperatively the bile drainage from the T-tube gradually diminished and became colorless. Spontaneous hemorrhage occurred from many sites, and the patient succumbed Nov. 2, 1955, five and one-half years after the onset of his symptoms.

Fig. 6A (Case 2).—Cholangiogram on June 6, 1953, showing visualization of common duct, gallbladder, and right hepatic duct. Negligible traces of dye in the left hepatic ductal system indicate obstructive lesion, thought to be cicatricial "sclerosing cholangitis."

At autopsy the liver was found to be enlarged, green, and rubbery. Beneath a hematoma in the right lobe there was a large zone of acute hemorrhagic infarction. The thin-walled gallbladder was enveloped in connective tissue and distended by grayish mucopurulent exudate. The common duct was thick-walled, and its lumen contained a small amount of bile. Above the confluence of the hepatic ducts and proceeding into the hilar liver substance for a distance of 2 cm., there was a dense, grayish-red mass of scarred neoplastic tissue, which stemmed from the left hepatic duct and which extended to the junction with the right hepatic duct and liver hilus (Fig. 5B). Intrahepatic biliary radicles in the left lobe were distended and contained purulent exudate. The branch of the portal vein accompanying the left hepatic duct was also the seat of suppuration. There was no evidence of metastasis, and the periductal cicatrix in the liver hilus was free of neoplasm. Only the

Fig. 6B (Case 2).—Cholangiogram one year later, on May 7, 1954, showing no significant change.

left hepatic duct and immediately contiguous tissue contained well-differentiated adenocarcinoma. The final diagnoses were as follows: (1) adenocarcinoma, left hepatic duct, with obstruction; (2) hydrohepatosis, left lobe, with suppurative cholangitis; (3) massive hepatic infarction, subcapsular, right lobe; (4) suppurative pylephlebitis; (5) empyema of gallbladder with cystic duct stricture; (6) lower nephron (bile) nephrosis; (7) lobular pneumonia.

Fig. 6C (Case 2).—Serial cholangiogram on Nov. 18, 1955, after last operative exploration. Progression of the obstructive biliary ductal lesion is evident. Gallbladder and common bile duct are essentially normal.

Case 3.—A 55-year-old white woman entered the hospital Dec. 19, 1953, after three weeks of jaundice, pruritus, anorexia, and vomiting. Laparotomy revealed the gallbladder to be filled with large calculi, one of which appeared impacted in the cystic duct. The gallbladder was removed, and the common duct was opened and explored. Probes were passed freely into the duodenum and both hepatic ducts. No stones were encountered, and bile emerged from above. A T-tube was inserted into the common duct, and a free flow of bile continued until the tube was withdrawn on the ninth postoperative day.

Fig. 7 (Case 3).—Operative cholangiogram showing partial obstruction and poor filling of hepatic ductal radicles.

Two weeks after discharge, the patient had severe, knife-like epigastric pain, and icterus reappeared. On the day of entry there were chills and fever. The abdomen was reexplored and the common duct found to be thick-walled and narrowed, and its lumen contained no bile. A dilator was passed freely into the duodenum but met some obstruction in the hepatic duct. It passed with minor difficulty, however, after which thick green pus drained from above. A T-tube was inserted. For a few days postoperatively the temperature was septic but returned to normal as the jaundice lessened. It was noted that bile drained around, but not through, the T-tube. The stool remained acholic. A cholangiogram via the T-tube revealed the opaque medium entering the duodenum readily,

but neither the upper area of the tube nor the hepatic ducts were visualized.

On Feb. 4, a third operation was carried out. No bile drainage occurred after the removal of the T-tube. Using dilators, passage into the liver through the channel of the right hepatic duct was possible, but no bile emerged. An intraductal curettement produced a small amount of tissue, which microscopically revealed adenocarcinoma. An operative cholangiogram again revealed ready entrance of dye into the duodenum. A few large intrahepatic biliary radicles were demonstrably dilated, but filling of the finer channels was poor (Fig. 7).

Following operation, there were copious drainage of bile from the T-tube, transitory diminution of jaundice, and symptomatic improvement. The flow gradually lessened, however, and jaundice again deepened. The patient died at home four and one-half months after the last operation and six months after the onset of symptoms. There was no autopsy.

Comment

It is well recognized that obstruction of the bile ducts may be produced by stone, traumatic stricture, or tumor. Obstruction due to slowly developing inflammation of the ducts has also been described as "sclerosing cholangitis." Although the concept of this latter type of obstruction has been accepted by many surgeons as a definite entity, many pathologists question its validity, pointing to the fact that accurate and complete pathologic confirmation has not been presented. In most of the cases in which it has been described a previous operation has been performed, with probing or other trauma to the ducts. One of the early reports of this lesion is that by Judd,[7] in which he estimated that 16 of 64 strictures of the common bile duct were due to cholangitis, and that in 15 more the etiologic factor may have been cholangitis. Numerous articles and individual case reports have been presented since that time, with little or no pathologic verification. The possibility exists that strictures thought to be due to this condition may actually be caused by sclerosing and slowly growing adenocarcinoma of the major intrahepatic bile ducts.

Accurate differential diagnosis of primary intrahepatic biliary carcinoma and benign "sclerosing cholangitis" may be exceedingly difficult. The major ductular elements of the biliary system, including those of the gallbladder and pancreas, have a similar mucosal coat. The lining layer consists of simple columnar epithelium with secretory capacity, but normally without goblet-cell characteristics.[3] In the absence of a muscularis mucosae, the cells, with an intermediate stromal layer of variable thickness, rest directly upon such muscular coat as may exist in a given area.[8] On occasion, there are anatomic insinuations which allow the mucosal folds to interdigitate with the muscularis, as in the case of the Aschoff-Rokitansky sinuses of the gallbladder.[9] In the major ducts there are sacculi with irregular distribution, comprising a periluminal system of glands.[8,10] In the presence of cicatrizing residua of inflammatory disease, the mural distortion, attendant fibrosis, and displacement of these acini may interpose some difficulty in distinguishing from invasive glandular carcinoma.[2] Loquvam and Russell[11] have discussed a similar problem in interpretation encountered in the region of the ampulla of Vater. This was undoubtedly the situation in the initial biopsy material in Case 1, although later consideration of the sections revealed clear evidence of neoplasm (Fig. 1*A*). The illustrations indicate the difficulty which may occur under such circumstances. Proper histologic appraisal requires close liaison between surgeon and pathologist. Contributory historical detail and accurate location of the biopsy site are essential for the pathologist's evaluation. Even with these data, sharp distinction between well-differentiated adenocarcinoma and the distortions of inflammatory stricture, or so-called "sclerosing cholangitis," may be difficult.

The prognosis of carcinoma of the extra- and intrahepatic biliary radicles is recorded as grave. With few exceptions death is said to occur rapidly, and there are uncommon survivals beyond one year after

the onset of symptoms.[1-4,9] The average survival time of Niebling, Dockerty, and Waugh's series [16] was three to four months after operation and five months after the onset of jaundice. The prolonged survival periods of three and one-half and five and one-half years, respectively, for Cases 1 and 2 are unique, and we have found no similar reports. Although widespread peritoneal metastasis ultimately occurred in Case 1, Case 2, after five and one-half years, revealed no extension of the carcinoma beyond the immediate area of the primary site. Of particular interest was the period of marked improvement for almost two years after dilatation of the obstructed segment of the left biliary ductal system in Case 2. The occurrence of such unusual survival coupled with equivocal biopsy findings of malignant neoplasm may lead the surgeon to discount the possibility of malignant neoplasm. This entered into clinical considerations rather prominently in Cases 1 and 2. Indeed, when metastatic carcinoma supervened in Case 1, consideration was given temporarily to the concept of ductal neoplasm engendered by prolonged nonneoplastic obstruction. This has been shown to occur in experimental animals [4,14] and has been suspected in human subjects.[12-14]

The relation of this lesion to biliary calculi is also of some interest. Gallstones have been described in relation to carcinoma of the extrahepatic biliary ducts in approximately 33% of the cases and in 70% to 90% of patients with primary carcinoma of the gallbladder.[5,15,16] Gallbladder stones were present in only one of our three cases of sclerosing carcinoma of the major intrahepatic bile ducts (Case 3), giving an incidence of 33%, similar to that recorded for extrahepatic biliary-duct carcinoma.

The ages of 32, 43, and 55 years suggest that younger persons are more susceptible to this form of intrahepatic ductal carcinoma than to the extrahepatic type. The average age reported for the extrahepatic type is 55.6 years,[15,16] while the average age of the three cases presented here is 43.3 years.

Symptoms and signs associated with this lesion varied with its duration and stage of development. The onset was insidious and of short duration. It was characterized by progressive jaundice, mild epigastric pain, anorexia, nausea, vomiting, and marked loss of weight. Fever occurred in two of the three patients at the time of admission to the hospital. As the process progressed, pruritus, loss of weight, marked jaundice, fever and chills, and anorexia became more marked. Finally, evidence of liver insufficiency supervened, including coma, spontaneous hemorrhage from the mucous membranes, lower nephron nephrosis, multiple liver abscesses, and terminal pneumonia.

The nature of this disease may easily be overlooked during operation. Since the gallbladder and common bile duct are small, the surgeon may conclude erroneously that the cause of the jaundice is hepatitis. Operative cholangiograms may be helpful in demonstrating the obstruction of the intrahepatic biliary tree.[19]

In addition to technical and diagnostic difficulties, the surgical management of this lesion presents other problems. Hepatojejunostomy should be considered as a palliative procedure for the relief of jaundice and its associated symptoms and for the delay in the development of intrahepatic complications, such as biliary cirrhosis, cholangitic abscesses, and suppurative pylephlebitis. From our experiences in Cases 1 and 2, hepatojejunostomy would have to be utilized early in the course of this tumor to be accomplished or to be effective. The possibility of resection of the left lobe of the liver should be kept in mind for early lesions located in the intrahepatic portion of the left hepatic duct.

Case 1 offered a unique opportunity to trace the pattern of the lesion of the hepatic duct over a three-year period of obstruction by means of multiple biopsy specimens, supplemented by tissue procured at necropsy. The initial needle biopsy specimen revealed obstructive bile stasis, characterized by centrilobular capillary bile plug for-

mation [17] without significant change in the parenchyma. The portal areas were enlarged and edematous and exhibited stellate configuration. The bile ducts contained minor evidence of intramural exudate, and there was early ductular proliferation (Fig. 2A).

Tissue procured one year later revealed that the pseudoangiomatous ductal pattern had progressed strikingly and the enlarged portal areas had extended to the point of interconnection with resulting perilobular arrangement. The picture was that of an unusually florid biliary cirrhosis (Fig. 4A).

After an interval of another year, the last liver biopsy specimen was obtained. Portal and periportal collagenization had become manifest. Remnants of ductular budding were persistent, but much less prominent than a year earlier. Interlobular ductules were recognizable, but these were small, narrow, and seemingly compressed by periductal cicatrization.

At autopsy, three years after the initial sample, the pseudoangiomatous ductular pattern had disappeared and the liver was frankly cirrhotic, narrow, and relatively acellular, with fibrous strands interconnecting portal areas and arrayed in perilobular fashion (Fig. 4B). Persistent ductules were few, attenuated, and obviously obliterated by the cicatrizing process. Were it not for suppuration and bile stasis and the knowledge of the nature of the lesions encountered during the development of this process, it would have been difficult to distinguish the cirrhosis from that commonly ascribed to long-standing, nonobstructive hepatitis.

Summary

Our experiences with three patients having sclerosing adenocarcinoma of the major intrahepatic bile ducts are presented. These cases have been unusual in our experience and have been characterized by an insidious development, a clinical similarity to the so-called "sclerosing cholangitis," repeated difficulties in establishing the correct diagnosis from biopsy tissues, and relative inaccessibility of the lesion to surgical approach.

The surprisingly long survival times in Cases 1 and 2 of three and one-half and five and one-half years, respectively, after the onset of symptoms, and the period of freedom from symptoms for two years postoperatively in Case 2, suggest the possibility that other strictures of the hepatic ducts, thought to be caused by "sclerosing cholangitis," might be similar instances of slowly progressing and obscure carcinoma of the major intrahepatic bile ducts. The likelihood of this possibility is further emphasized by the experiences of the various pathologists involved in these three cases in making an accurate microscopic differential diagnosis between primary intrahepatic biliary adenocarcinoma and benign "sclerosing cholangitis" until death and autopsy.

The surgical management of this neoplasm also presents many technical and therapeutic problems. Palliative hepatojejunostomy is recommended early for the relief of jaundice, before the development of intrahepatic complications, such as biliary cirrhosis, cholangitic abscesses, or suppurative pylephlebitis. Resection of the left lobe of the liver should be considered for lesions located in the intrahepatic portion of the left hepatic duct.

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DISCUSSION

DR. MAX M. ZINNINGER, Cincinnati: The chief comment that I would like to make on these cases is one that Dr. Altemeier has already mentioned, namely, that we were not sufficiently aggressive in our efforts to relieve the obstruction of the ducts. When there was failure to secure adequate drainage of bile by direct attack on the major ducts at the hilus, it now seems to me that an attempt to isolate and anastomose ducts at the periphery (by a procedure such as that described by Longmire) was indicated, and rather promptly. In Case 1, for which I am principally responsible, this was attempted, but only after a year of more or less complete biliary duct obstruction. This failed because in this long interval structural changes had occurred in the liver which led to the surgery being of no help. If it had been attempted 9 to 10 months earlier, it might have been more successful. In Case *2* such an attempt was never made, although it was considered and discussed on several occasions, but for one reason or another was never undertaken. In retrospect, it seems that with the localized nature of the cancer in this case cure might have been obtained by left hepatic lobectomy. In both Case 1 and Case *2* we were under the misapprehension that the lesion was a benign or an inflammatory stricture, and under such conditions one would scarcely be justified in such a radical procedure.

In recent years a number of case reports have appeared in the literature of so-called benign intrahepatic stricture of the bile ducts, discovered by operative cholangiography and treated by dilatation of the stricture. In many of these cases the cholangiograms resemble closely those which were obtained in Case *2*. In most of these reports the patients had been followed for less than two years. In Case *2* the patient remained well for more than two years after partial gastrectomy and dilatation of the stricture, only to die three years later with carcinoma of the ducts. This makes one wonder whether all of the cases reported are really benign strictures, or whether, if more adequate follow-up studies were available, some or many of the strictures might turn out to be due to slowly growing cancer of the ducts. It seems advisable, therefore, in such cases to make a determined effort to obtain adequate material for pathologic study, either by curettage of tissue which can be sectioned or by obtaining fluid or smaller amounts of tissue for cytologic study.

DR. TILDEN EVERSON, Chicago: As Dr. Altemeier has pointed out in this well-documented paper, accurate differentiation between the sclerosing type of biliary adenocarcinoma and sclerosing cholangitis is frequently difficult, and sometimes impossible, from microscopic examination of biopsy material. Consequently, biliary adenocarcinoma cannot be completely ruled out as an etiologic possibility in biliary strictures which are not associated with previous operative trauma, despite a microscopic diagnosis of biopsy tissue as inflammatory.

A case I have followed during the past two years confirms in retrospect many of the features presented in this paper. The patient was a 62-year-old man who was admitted to the hospital in February, 1955, with a two- to three-week history of jaundice. At operation a marked thickening and induration was noted in the region of the

common hepatic duct, extending proximally as far as the duct could be palpated. However, probes were passed readily into the duodenum and up into the hepatic ducts. A portion of the duct was excised, and a frozen section was diagnosed as possible carcinoma. A T-tube was inserted. However, the paraffin sections of the biopsy material were interpreted as inflammatory tissue with no evidence of cancer. The surgeon remained convinced of the neoplastic condition of the lesion.

The patient was readmitted in September, 1955, when he was first seen by me. Because his general condition was good and he had gained weight, a second operation was done, and at this time it was found that the mucosa of the common hepatic duct was eroded and the wall was thickened. A full-thickness biopsy specimen of this area was reported as inflammatory tissue on frozen section, and this diagnosis was confirmed by paraffin sections. A T-tube was reinserted and removed seven weeks postoperatively.

In December, 1955, the patient again returned to the hospital with recurrent jaundice and a fistula at the site of the previous T-tube. At operation this time the bile duct area was stony-hard, and frozen section of the biopsy specimen from this area revealed sclerosing adenocarcinoma. This diagnosis was confirmed by paraffin sections. The dissection was continued along the course of the obliterated hepatic ducts deep into the liver, where a duct was encountered which had thickened walls. This was anastomosed to a Roux-Y limb of jejunum.

Although the postoperative course was relatively uneventful, on follow-up examination, six months later, jaundice was present, and the patient died approximately 18 months after the first operation and 19 months after the onset of jaundice. Unfortunately, since the patient died outside the hospital, an autopsy was not performed.

In order to obtain further information concerning the relative incidence of sclerosing obliterative cholangitis and sclerosing adenocarcinoma of the bile ducts, I would suggest that those who have had patients come to autopsy with a diagnosis of sclerosing cholangitis might ask their pathologists to review, and possibly resection, the pertinent material in light of the concepts presented in this paper.

DR. JOHN T. REYNOLDS, Chicago: I am enthusiastic about Dr. Altemeier's idea of doing an hepatic lobectomy, provided the carcinoma in the common duct is limited to one lobe of the liver.

I have seen only one patient with carcinoma of the common duct, and I was fortunate at that time to have a very bright resident helping me. At his suggestion we introduced a heavy polyethylene tube through the area of the common duct, which was surrounded by carcinoma. This tube was inserted in such a manner that the upper end was in the dilated proximal duct and the distal end in the duodenum. With such an arrangement the patient's jaundice was relieved, and when she died, 19 months later, from generalized carcinomatosis, she had developed no jaundice.

DR. JOHN L. KEELEY, Chicago: I should like to apologize for discussing two successive papers, but this is a very interesting subject, and I merely rise to point out some facts about a patient whom we after an uneventful cholecystectomy, this patient encountered a couple of years ago. Six months became jaundiced. We explored the area and could find no common duct at all. Three weeks later, when no fistula developed after this exploration, we performed a Longmire procedure, which kept the patient free from jaundice for 11½ months. Autopsy revealed an adenocarcinoma involving the junction of the right and left hepatic ducts, and during that period of survival only the left lobe of the liver had been drained. The right lobe had a number of small abscesses and one large abscess, and the terminal event was an esophageal hemorrhage. This case does not fit into the age group that Dr. Altemeier has presented, but the Longmire procedure certainly solved the problem of jaundice for this patient and allowed her to survive for one year.

DR. WILLIAM A. ALTEMEIER, Cincinnati: I would like to stress two points.

The diagnosis in two of these cases was in doubt for periods of three and one-half and five and one-half years, respectively, even though repeated biopsy specimens of the involved area had been taken. In one case it was in doubt until the time of autopsy, when the permanent microscopic sections were reviewed.

This fact emphasizes the possibility that many other cases of sclerosing cholangitis may be instances of slow-growing, sclerosing carcinoma of the intrahepatic bile ducts.

I would like to request that any of you having cases diagnosed as obliterative or sclerosing cholangitis of the intrahepatic bile ducts follow them carefully and obtain autopsy information, if possible, to determine whether the process is actually an inflammatory one or a sclerosing carcinoma.

We would also welcome sections of material obtained from any cases of this type for our review.

Relation of Obstructive Jaundice to Adrenal Function

JOHN B. FULLER, M.D., and JOHN H. SCHNEEWIND, M.D., Chicago

The adrenal gland responds to the stress of surgical procedures by an increase in cortical hormone output, and about 80% of these steroids are reported to be in the form of hydrocortisone—one of the 17-hydroxycorticoids. These substances are related to carbohydrate and protein metabolism, as well as having anti-inflammatory and antipyretic properties. The other 20% of adrenal output includes hormones, such as aldosterone, which primarily affect electrolyte and fluid balance.

Despite lack of knowledge of the way in which these hormones act on cells and of their disposition in body fluid compartments, it is becoming increasingly clear that there is a direct relation between liver function and adrenal corticoid metabolism. It has been shown[1] that after infusions of hydrocortisone in normal subjects 50% of the hydrocortisone had left the plasma in 114 minutes. In patients with cirrhosis, however, it required 160 to 800 minutes for 50% of the steroid to leave the plasma. Brown and associates[2] gave intravenous hydrocortisone to 11 normal subjects and to 12 patients with liver disease. Six hours after the infusion the plasma levels of the patients with liver disease were over three times as high as those of the normal subjects. The rate of disappearance of the hydrocortisone was inversely proportional to the degree of liver damage as measured by sulfobromophthalein (Bromsulphalein) retention. These investigators have cited these data as evidence of disturbed corticoid metabolism and decreased hormone output due to liver disease.

Since some hepatic dysfunction must invariably accompany obstructive jaundice, we are reporting the evidence for diminished adrenal corticoid output in 13 patients with obstructive jaundice. Included are comparative studies on six normal patients.

Method

Our plan of investigation was to compare urinary 17-hydroxycorticoid output in the two groups of patients during three periods. The first period was prior to operation and during which the patient was not on any form of steroid therapy. This period was used as "base line," i.e., as representing the normal output for that patient under ordinary circumstances. The second period was following administration of 40 units of corticotropin in the form of a gel every 12 hours for four doses. The preparation is given intramuscularly and has a duration of action of about 24 hours. This provides an appreciable stimulus to corticoid secretion and gives some indication of the capacity of adrenal response under stress. The final collecting period was during the day of operation and for the first three postoperative days. Average daily outputs for the base-line and corticotropin periods were calculated by dividing the total output during the respective two-day collecting periods by the total number of days of collection. Average values for the day of operation and the three postoperative days were obtained by dividing the total output of the respective day by the number of patients studied.

Under the conditions of this study, normal patients were considered to be those with no evidence of obstructive jaundice, liver disease, or adrenal insufficiency, nor were they receiving any form of steroid therapy. The jaundiced patients were a more heterogeneous group in that they included patients with varying degrees of biliary obstruction and with gradations of hepatic dysfunction.

The method used for the determination of urinary total 17-hydroxycorticoids is that of Reddy, Jenkins, and Thorn.[3] Steroids are ex-

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Dr. H. C. Batson gave valuable assistance in statistical analysis of our data. Miss Lynn Miller gave excellent technical help.

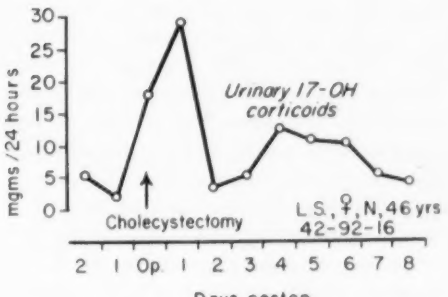

Fig. 1.—Normal steroid response following cholecystectomy. Urinary 17-hydroxycorticoid levels were normal prior to operation, with a prompt rise to 29 mg. on the first postoperative day. Our average normal for the first postoperative day was 24 mg.

tracted with butanol after adjustment to pH 1[4,5] and quantitated by the Porter-Silber reaction.

Results

The data obtained indicate that the patients with obstructive jaundice excreted significantly smaller quantities of urinary 17-hydroxycorticoids during all three collecting periods, i. e., prior to operation, after administration of corticotropin, and during the immediate postoperative period.

Adrenal Response of Normal Patients.

A normal steroid response following operation is shown in Figure 1. The 46-year-old Negro woman entered the hospital for an elective cholecystectomy. The urinary steroid levels were normal prior to operation, and there was a prompt increase following operation to 29 mg. on the first postoperative day. Recovery was uncomplicated.

The response of a normal patient to a preoperative corticotropin test and to operation is shown in Figure 2. There was an immediate response to corticotropin, with a peak of 34 mg. on the second day of therapy. Following a right hemicolectomy and excision of a long-standing fistula, the urinary steroids rose to a peak of 26 mg. on the third postoperative day. The decrease in 17-ketosteroid output during this period represents a dissociation as compared with 17-hydroxycorticoid levels, which is not uncommon. The patient did well after operation. Her weight rose from 90 to 160 lb. (40 to 72 kg.) 16 months after operation. The long period of chronic infection and malnutrition was still evident in the form of abnormal thymol turbidity and cephalin flocculation tests.

The next patient illustrates an active adrenal response following operation with recovery despite intraperitoneal bleeding and a wound dehiscence. The patient did not have obstructive jaundice, and there was no evidence of liver disease prior to operation. This 59-year-old white woman en-

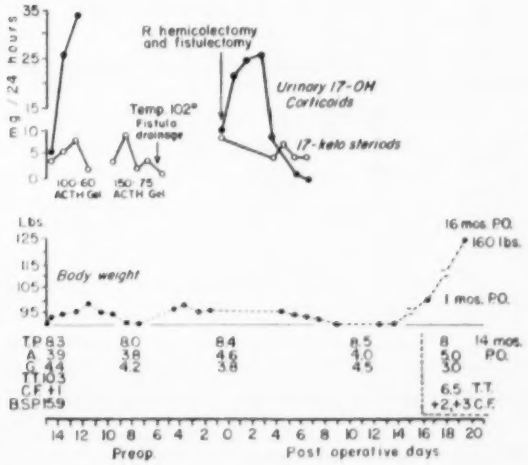

Fig. 2.—Good steroid response despite chronic infection and malnutrition in a woman aged 29. Urinary 17-hydroxycorticoid output of this malnourished patient increased both after corticotropin and after operation. The 34 mg. level after corticotropin compares with our average of 31 mg. for nonjaundiced patients. Peak rise to 26 mg. on the third postoperative day compares with the normal high of 24 mg. on the first postoperative day. The delayed peak may have reflected moderate hepatic dysfunction.

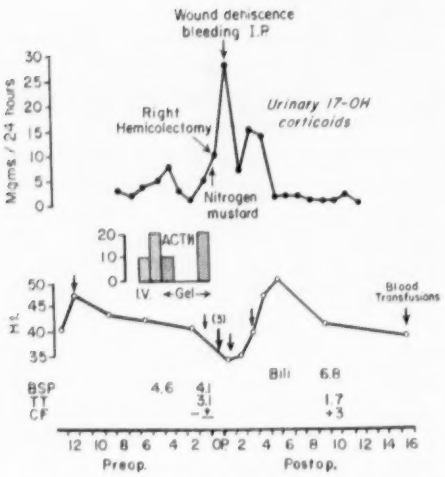

Fig. 3.—Active adrenal response with recovery in a depleted patient. Prompt increase in urinary 17-hydroxycorticoids to 26 mg. on first postoperative day compares with average normal of 24 mg., indicating no adrenal depression by mechlorethamine (nitrogen mustard) instilled intraperitoneally at time of operation. There is also evidence of increased adrenal output following small doses of corticotropin.

tered the hospital because of postprandial epigastric distress, which had been present for years. A barium examination of the stomach revealed a gastric ulcer. At operation the duodenum was normal, and the gastric ulcer was almost completely healed. Examination of the intestine, however, revealed a 2 cm. lesion of the cecum, which proved to be an adenocarcinoma. A right hemicolectomy was performed, after which approximately 4 mg. of mechlorethamine hydrochloride N. F. (nitrogen mustard) was put in the peritoneal cavity as a prophylaxis against tumor emboli. Points of interest in the graph (Fig. 3) are a slight increase in urinary steroid output following small injections of corticotropin, indicating, perhaps, a sensitive adrenal response and absence of any obvious depression of adrenal function by the single mechlorethamine instillation.

Adrenal Response of Patients with Common-Duct Obstruction.—The next case is an example of a good response to a preoperative corticotropin load, but a rather minimal urinary corticoid output following common-duct exploration and a transduodenal sphincterotomy (Fig. 4). This 63-year-old white woman had a cholecystectomy and choledochostomy at another hospital four months prior to admission. Following this operation the patient experienced several attacks of acute pancreatitis, characterized by abdominal pain, fever, and elevated serum amylase readings. A cholangiogram via the T-tube showed marked dilatation of the common duct. Several attempts were made to clamp the T-tube, but each time the patient experienced a recurrence of pain and fever. There was evidence of hepatic dysfunction in the form of elevated sulfobromophthalein and positive cephalin flocculation tests. At operation a cystic dilatation of the proximal common duct and a stenosis of the sphincter of Oddi were found. Sphincterotomy was performed. The data in Figure 4 show a good response to the corticotropin-loading test despite the evidence of liver damage. An output of 66 mg. was recorded on the second day of corticotropin administration. The presence of a T-tube facilitating biliary drainage was probably a factor. The urinary steroid output after operation was minimal, evidence, perhaps, of a rather

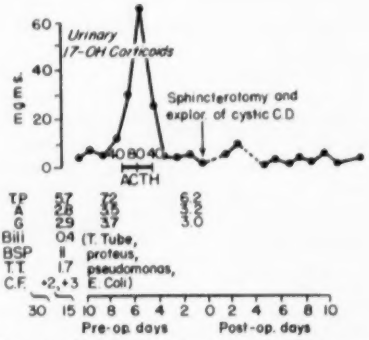

Fig. 4.—Urinary 17-hydroxycorticoid response to preoperative corticotropin test and to operation. This 63-year-old white woman developed pancreatitis and stenosis of the sphincter of Oddi following cholecystectomy and choledochostomy. The high output of corticoids on corticotropin contrasts with a minimal rise following operation. A possible explanation is that the patient had a rather narrow hepatic reserve, barely adequate to carry the load of anesthesia and operation. Recovery was satisfactory.

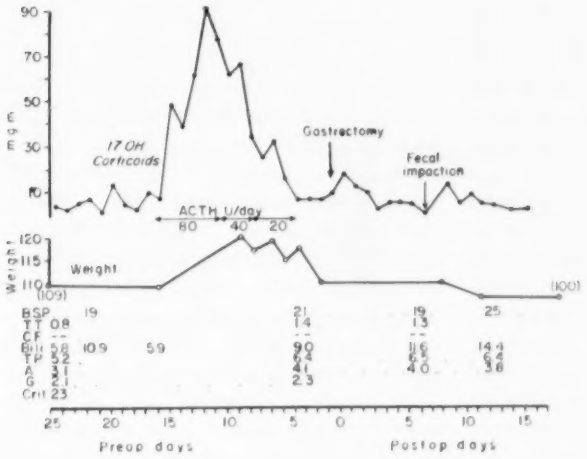

Fig. 5.—Urinary 17-hydroxycorticoid pattern of a woman aged 63 with biliary cirrhosis due to destruction of the common duct by a duodenal ulcer. The course of corticotropin preoperatively resulted in transient weight gain, euphoria, and improved A/G ratio. The patient tolerated a rather difficult gastrectomy well.

narrow hepatic reserve and a diminution of conjugation of adrenal steroids by the liver.

Adrenal response to large doses of corticotropin prior to operation and urinary corticoid output following operation were studied in a patient with biliary cirrhosis complicated by peptic ulcer of the duodenum (Fig. 5). The history of this 63-year-old white woman is rather complicated but, in essence, involves the onset of jaundice, intermittent in type, following cholecystectomy. She subsequently experienced episodes of gastrointestinal bleeding, necessitating frequent blood transfusions. The patient was admitted to Research and Educational Hospitals, and exploration of the biliary system was attempted but had to be abandoned because of profuse bleeding, probably due to portal hypertension. A splenorenal shunt was then performed at a subsequent operation. The patient continued to have positive tests for blood in the stools despite the shunt, and icterus persisted. She was readmitted to the hospital several weeks following the shunt, at which time she was moderately jaundiced, malnourished, and had marked hepatomegaly. The hematocrit reading was 23; bilirubin, 5.8 mg. per 100 cc.; thymol turbidity and cephalin flocculation normal, tests total proteins 5.2 gm. per 100 cc., and sulfobromophthalein 19 per cent (Fig. 5). The stools continued to be strongly positive for blood, and a barium examination showed a marked deformity of the duodenal bulb. Because the patient failed to gain weight in the hospital, an intensive course of corticotropin was given, despite the evidence of an ulcerating lesion in the gastrointestinal tract. The corticotropin caused an immediate improvement in appetite; euphoria, rather typical of patients on steroids, and a 10 lb. (4.5 kg.) weight gain, a large part of which was due, no doubt, to water retention. Despite the fact that much of the weight was lost after cessation of corticotropin, we were impressed with the improvement in mental attitude and general well-being. The serum proteins increased to 4.1 gm. of albumin and 2.3 gm. of globulin per 100 cc. and remained at this level after operation.

The urinary output of steroids, as shown in Figure 5, lagged slightly after commencement of corticotropin, but then rose to a peak of 90 mg. In contrast, the output following operation rose only to 20 mg. on the day of operation and then gradually fell to lower levels. At operation, a very large duodenal ulcer was found. Part of the ulcer bed was the undersurface of the right lobe of the liver. Furthermore, it developed that the ulcer had eroded into the common bile duct and that the bile was

draining from the proximal common duct directly into the ulcerated area of the duodenum. A partial gastrectomy of the Bancroft type was performed, which the patient tolerated well. The patient's postoperative course was uneventful, but the icterus was slow in subsiding.

The following example of a minimal urinary corticoid response after operation was that of a 66-year-old white woman who had undergone cholecystectomy, removal of a common-duct stone, and sphincterotomy for stenosis of the sphincter of Oddi, three years prior to admission. She was well for a year, but then began to have jaundice, pruritus, and dark urine for three- or four-day periods every two to three weeks. On the evening of admission she experienced a shaking chill and a temperature of 103 F.

At operation a recurrence of the stenosis of the sphincter of Oddi was found. Clear bile gushed from the opening when it was stretched; accordingly, the sphincter was cut for about ½ in. (1.25 cm.) upward. The patient did very well after operation except for a transient rise in serum bilirubin and sulfobromophthalein retention, probably due to edema at the sphincter (Fig. 6). Culture of the bile revealed only a few enterococci and Aerobacter aeorgenes. The urinary corticoid output on the day following operation was only 7 mg., rose slightly on the third postoperative day following transient obstruction at the sphincter, due presumably to edema, and then subsided to low normal levels. The patient recovered without further incident.

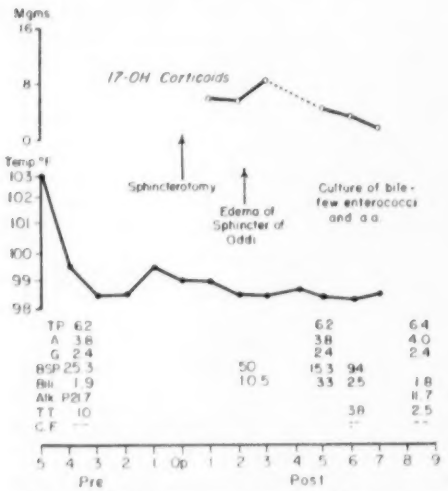

Fig. 6.—Rapid recovery after sphincterotomy despite hepatic dysfunction and portal hypertension. Typical postoperative urinary corticoid output of patient, aged 66, with obstructive jaundice. The 7 mg. output on the first postoperative day compares with an average of 24 mg. for normal patients. The rise on the third postoperative day probably was due to a transient edema of the sphincter of Oddi.

Base-Line Levels.—By this term we mean the 24-hour urinary 17-hydroxycorticoid output of a patient prior to operation. These patients are in a reasonably basal state from an adrenal standpoint, i. e., are not on corticotropin or steroid therapy and are not under undue stress. The following figures were obtained on two consecutive, complete collections. The average base-line steroid output for the normal (nonjaundiced) patients was 10 mg. per 24 hours. (Two standard deviations equal ±3.5.) This is similar to data on normal patients reported by others.[3] For the jaundiced patients the average base line was 4.5 mg. per 24 hours (2 s. d. = ±1.7).

Adrenal Output Following Corticotropin.

For the normal patients the average daily output after corticotropin was 31 mg. per 24 hours (2 s. d. = ±13.2). After corticotropin the jaundiced patients had an average daily output of 17.5 mg. (2 s. d. = 9.2). These data are graphically illustrated in Figure 7. Statistical analyses were done on patients with complete collections and included eight patients.

The base-line and postcorticotropin outputs for normal and jaundiced patients were subjected to an analysis of variance and were found to be significant at the 1% level ($P = 0.01$).

Adrenal Output Following Operation.—On the day of operation the average urinary 17-hydroxycorticoid output for normal patients was 15 mg. This increased to 24 mg. on the first postoperative day and was 10 and 15 mg. on subsequent days. The

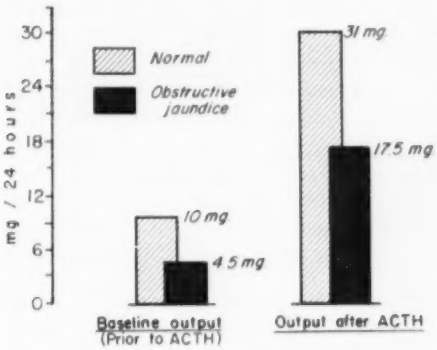

Fig. 7.—Effect of corticotropin on average daily urinary 17-hydroxycorticoid output in normal and jaundiced patients. Base-line levels represent average output prior to a two-day corticotropin test. Daily output was also measured during the test period in which 80 units of corticotropin gel was given daily for two days. The average daily output of the normals was 10 mg., or more than double the average base line of the jaundiced patients (4.5 mg.). The average output after corticotropin for the normals was also appreciably higher than that of the jaundiced patients.

jaundiced patients averaged 9 mg. on the day of operation and 12, 9, and 9 mg. per 24 hours on the first, second, and third postoperative days, respectively. These figures are illustrated in Figure 8. The values were subjected to an analysis of variance and were significant at the 5% level ($P = 0.5$). Only complete four-day collection figures were used for the statistical analysis.

Comment

While it is true that most methods of urinary steroid analysis measure only 30% to 50% of the total output of the gland, the consistency of the data enables one to get some idea of the trend of adrenal response under various circumstances.

Our study of base-line adrenal output showed that patients without obstructive jaundice had more than double the output of the jaundiced patients. This is consistent with a previous report that patients with liver disease (cirrhosis, etc.) excreted 30% less 17-hydroxycorticoids in the urine than do normal patients.[2] The importance of this lies in the fact that it may signify depression of adrenal function, which, while not severe enough to affect the patient under ordinary circumstances, might endanger his life in a situation of severe stress, such as a major operation.

Before commenting on the adrenal response to corticotropin, we might review situations in which we find this drug to be most useful. By studying basal output and then administering large doses of corticotropin gel during a 48-hour period, some indication of the patient's functional adrenal reserve may be obtained. Some investigators prefer a smaller dose administered in a continuous infusion for eight-hour periods, but for ease of administration we prefer the twice daily intramuscular method. We have noted that adrenal output following administration of corticotropin gel is often much higher than output following even a severe operation; this is especially true when the corticotropin is given for a 5- or 6-day period. It may be that the sustained stimulus provided by the intramuscular preparation is more potent in producing high outputs than is the relatively short period of operation. At any rate, recovery from operation is entirely consistent with urinary steroid levels which are appreciably lower than those seen following corticotropin

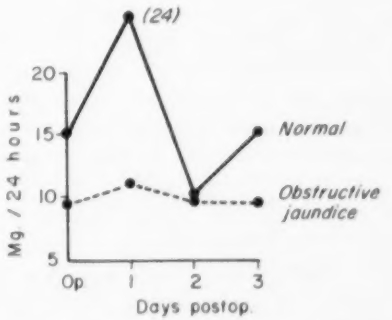

Fig. 8.—Effect of operation on urinary 17-hydroxycorticoid output in normal and in jaundiced patients. The average 17-hydroxycorticoid output for normal patients on the day of operation was 15 mg. This increased to a peak of 24 mg. on the first postoperative day, then fell to 10 and 15 mg. on the second and third days, respectively. In contrast, the jaundiced patients excreted 9 mg. on the day of operation and 12, 9, and 9 mg. on subsequent days.

therapy in the preoperative period; this is illustrated in Figure 5.

Many of our patients enter the hospital in a state of profound malnutrition, and it is here that we find corticotropin of great value in improving appetite and inducing a feeling of well-being. Despite the fact that some of the weight gain is often due to water retention, improved intake usually raises the serum protein levels and greatly improves operability. Not all patients respond in this fashion, and whether those that do are in reality suffering from a moderate adrenal insufficiency is a matter of conjecture. Improved methods of steroid analysis may help us answer this question. The effect of corticotropin in reducing fever may also be valuable when utilized judiciously. It might be noted that we rarely use corticotropin in cases where immediate operation is indicated, as, for instance, in a case of acute abdominal catastrophe with peritonitis. We prefer to take these patients to the operating room as soon as electrolyte, hydration, and hematocrit levels are restored and to rely on steroid therapy in the immediate postoperative period should it prove necessary. Other conditions in which we find corticotropin helpful preoperatively are various hematologic diseases, such as thrombocytopenic purpura, and miscellaneous conditions, including ulcerative colitis and regional enteritis. It must be realized that corticotropin may be dangerous in masking pain and muscle spasm of the abdomen, may cause perforation of a peptic ulcer, and should rarely, if ever, be given to patients with diabetes, hypertensive cardiovascular disease, Cushing's syndrome, pregnancy, or tuberculosis.

The patient who recently has been or currently is on steroid therapy and requires operation is a special problem in which corticotropin may be quite helpful from both a diagnostic and a therapeutic standpoint. Should urinary and plasma analyses reveal somewhat low levels, corticotropin may be started a few days prior to operation and continued until the patient is safely over the critical postoperative period. It should be noted that soluble hydrocortisone must be kept in the operating and recovery rooms for immediate use should the patient go into shock for which no ready explanation, such as blood loss, is apparent.

Data on Adrenal Steroid Output of Normal and of Jaundiced Patients

	Steroid Output, Mg/24 Hr.	
	Normal Patients	Patients with Obstructive Jaundice
Base-line levels	10	4.5
Following corticotropin	31	17.5
Following operation		
Day of operation	15	9
Postop. day 1	24	12
Postop. day 2	10	9
Postop. day 3	15	9

Our data on adrenal output of normal and jaundiced patients following corticotropin show a significant difference in response of the two groups and are illustrated in Figure 7. The jaundiced patients not only had lower base-line outputs and lower levels after corticotropin than the nonjaundiced patients, but also had significantly smaller outputs after operation, as is shown in Figure 8. These data are summarized in the accompanying Table. This information supports the current theory of a direct relation between hepatic function and corticoid metabolism and implies that the presence of obstructive jaundice may cause a depression of adrenal function which, while it does not affect the patient under ordinary circumstances, might under conditions of severe stress require adrenal replacement therapy.

Summary

Urinary 17-hydroxycorticoid levels on six normal (nonjaundiced) patients and 13 patients with varying degrees of obstructive jaundice have been determined. Three collecting periods were chosen. The first was a base-line period prior to operation and during which the patients were not receiving steroids. The second period was during administration of large doses of corticotropin gel and, finally, urines were collected

immediately after operation. The patients with obstructive jaundice had statistically significant smaller (about one-half) corticoid outputs during all three periods.

These data support the concept of a direct relation between liver function and steroid metabolism. They imply further that the presence of obstructive jaundice may cause a depression of adrenal function which under ordinary circumstances would not be obvious, but which under the stress of a heavy operative load might require immediate treatment with steroids, such as hydrocortisone.

Department of Surgery, University of Illinois College of Medicine.

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DISCUSSION

DR. HENRY SWAN, Denver: I am very much interested in this report and in the suggestion that perhaps patients with liver disease may need postoperative endocrine therapy.

The effect of liver disease on the metabolic response of the patient to trauma is an extremely interesting and important subject. However, since the liver has a profound effect on many facets of the metabolic economy of the body, a decision as to exactly what effect it is having on various parts of this metabolic change is very difficult.

Dr. Schneewind and Dr. Fuller have made a strong corroborative study of the fact that in patients with obstructive jaundice, breakdown or so-called conjugation of the free hormone is probably distinctly suppressed. Whether this has any real bearing on whether this patient needs active hormone, or is in fact deficient in active hormone, is not so clear.

The Porter-Silber chromogens which appear in the urine are 95% degradation products and only 5% hydrocortisone (Compound F). In the slides that you have seen these conjugates were the materials which were depressed.

I think it would be very important if, in association with these studies, one were to observe whether or not there was a change in the secretory response of the adrenal cortex, as well as a change in the degradation process of the hormone. We have recently studied some warm patients, Dr. Zollinger, and, with your permission, I should like to show two slides which illustrate some points about the immediate endocrine response to major surgery in warm subjects.

(Slide) These are the levels in the plasma of free circulating hydrocortisone, in contrast to the conjugated form in the plasma as determined by the Bongiovanni method, during the day of surgery and in the days following surgery.

First note the extraordinary speed of the response of the output of the free hormone in this early period, which is the midsurgery point (elected by the anesthesiologist who collected these specimens as the middle of the operation). You see already a very pronounced response, which crept upward during the rest of the day.

The conjugation in these patients also occurred very soon thereafter, and by the end of the surgical procedure (in this period shown here) it had already risen; and by the time of the recovery period it had achieved a very high level, later falling off again.

So in these normal patients who presumably do not have liver disease, conjugation was occurring rapidly, and it reached a peak by the evening of the day of surgery.

(Slide) This slide shows the response in the urine of these same patients. Here one sees, as was suggested in the paper, that a marked increase in the total Porter-Silber chromogens occurs right after the recovery period, in the period of 12 to 24 hours following surgery. This parallels, then, and follows somewhat in time, the conjugation which had been manifested by a rise in the blood stream levels.

Whether or not the patient who has a failure of conjugation is in fact deficient in any sense in the active component of this early endocrine phase of metabolic response to trauma is not yet clear. I hope Dr. Fuller and Dr. Schneewind will con-

tinue with this study and will give us some data on the actual secretory response of the adrenal cortex, as well as upon the fate of the hormone.

Dr. John H. Schneewind, Chicago: I should like to thank Dr. Swan for his comments, and I do believe that study of the plasma levels is essential to a more complete analysis of steroid output.

It might be noted that plasma levels are pretty much a matter of moment-to-moment check, and that the urine reflects perhaps the total picture at the end of the 24-hour collecting period.

We are now in a position to determine free, and possibly total, plasma corticoids, and we are proceeding with certain studies along those lines.

Obituaries

THOMAS G. ORR Sr., M.D.

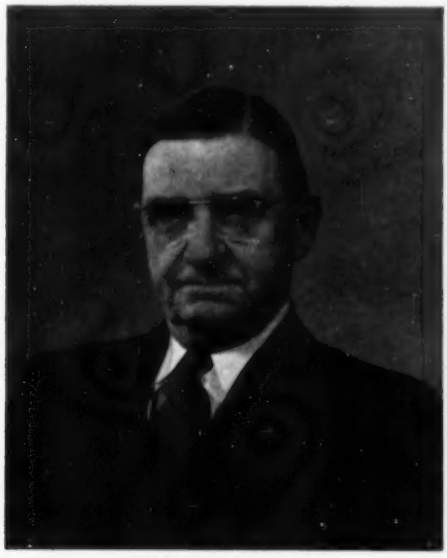
1884-1955

As a skilled surgeon, Dr. Thomas G. Orr Sr. brought comfort to many patients for 45 years. As a respected teacher, he passed on his skills and ideals to thousands of medical students and resident physicians. As a leader in the field of surgery, he left a strong imprint in its advancement. As a friend to all employees of the Medical Center, he left the memory of a great man with an endless capacity for humanism.

His patients and his associates always felt that no matter how busy Dr. Orr might be, he had time to talk, listen, and discuss. In helping with the administration of the School of Medicine, Dr. Orr made a contribution of balance and reason—he helped tie in all opinions toward the end of betterment of the school. He had a broad vision which recognized the contribution of each endeavor in the field of medicine.

He actually never knew retirement. He became professor emeritus in 1954. But he came to his office daily and worked on his writings, consulted with a few patients, and walked through the surgical suite to "see how things are going." Since 1951 he had been editor of *The American Surgeon*, and to this publication and the *Medical Center Bulletin* he devoted a great deal of time.

All articles in the January, 1956, issue of *The American Surgeon* are written by former students of his. With all his knowledge, one thing he did not learn was



THOMAS G. ORR, M.D.
1884-1955

how to retire. In October he presented a paper at a meeting of the Utah State chapter of the American College of Surgeons. On Nov. 4 he moderated a panel at a meeting of the regional Veterans' Administration Hospital in Kansas City. He was in his office the day before his death, on Nov. 19, 1955.

Thomas Grover Orr was born on a farm in Carroll County, Missouri, May 9, 1884. His parents were pioneers in Missouri, having come from Illinois in a covered wagon in 1875. Grover Orr attended a country district school until he was 15. He graduated from the Carrollton high school in June, 1903. That fall he entered the University of Missouri and was graduated with an A.B. degree in 1907. His college work was combined with first-year subjects in medicine at Missouri University. He was president of the glee club, the Q. E. B. H. senior honorary fraternity, and the senior class.

He entered Johns Hopkins University School of Medicine in 1907 and graduated with an M.D. degree in 1910. He served internships in Hudson Street Hospital (branch of New York Hospital), and at St. Mary's Free Hospital for Children, New York, from 1911 to 1913.

Dr. Orr began the practice of surgery in Kansas City in 1915. That same year he became a member of the staff of the University of Kansas School of Medicine. He was successively professor of bacteriology, instructor in surgery, assistant professor of surgery, and chief of the surgical outpatient clinic, from 1915 to 1924. He was professor of surgery and chairman of the department of surgery from 1924 to 1949. From 1949 to 1954 he was emeritus professor of surgery.

Dr. Orr served as a captain and major in World War I. He was a foundation member of the American Board of Surgery. He was a member of the American Medical Association and the Kansas State Medical Society; fellow of the American College of Surgeons (past governor), American Surgical Association (past president), Western Surgical Association (past president), Society of University Surgeons, Central Surgical Association, Société Internationale de Chirurgie, Southwestern Surgical Congress (past president), American Society for the History of Medicine, and Missouri Valley Medical Society (past president); past member of the Southern Medical Association, Kansas City Academy of Medicine (past president), Kansas City Surgical Society (past president), and Kansas City City Southwest Clinical Society (past president), and honorary member of the Chicago Surgical Society and the Southeastern Surgical Congress.

His fraternities were Beta Theta Pi, Phi Mu Alpha, Nu Sigma Nu, Alpha Omega Alpha, and Sigma Xi. He was listed in "Who's Who in the Middle West," "Who's Who in American Education," "World Biography," "American Men of Science," and "Who's Prominent in Medicine." He was the author of "Modern Methods of Amputation" and "Operations of General Surgery" (two editions), and author and co-author of more than 200 articles in surgical literature. Last June he was awarded an honorary degree of Doctor of Science from the University of Missouri.

LAWRENCE P. ENGEL, M.D.

Ainhum (Dactylosis Spontanea)

Report of a Case

MARTIN LLOYD NORTON, M.S.P.H., M.D.; ANGELO M. SALA, M.D., and MARTIN ELLIOT SILVERSTEIN, M.D., New York

Ainhum is from a verb in the Yoruba language meaning "to saw" or "to file."[42] The term was first applied to an unusual chronic disease affecting the pedal digits,[14] and sometimes the fingers,[11] by the African Negroes.

The condition was reported by Clarke in 1860.[16] He described it as "dry gangrene." It was not until da Silva Lima became aware of the disease in Brazil and reported on it in the *Medical Gazette of Bahia*[17] that the definitive entity was described and the name ainhum formally accepted. A pathologic study by Wucherer in 1872[54] marked the next phase in the elaboration of the entity. Facio, in 1924, contributed a roentgenologic demonstration to the description of the disease.[22]

Dactylosis spontanea occurs principally among the colored races, particularly Negroes, and mainly in men between the ages of 25 and 45.[14] Cases have been reported in white persons[40] and in females,[6,12,27,28,30,51] The disease may be familial; the lesion has been observed in several members of the same family.[17,20,34,39,41] It has been reported as endemic on the West African Coast, and in the Sudan, Algiers, Egypt, and the Transvaal. The disease has also been reported from Brazil,[17] Buenos Aires, British Guiana, the Panama Canal Zone,[50] India,[23] and Europe.[4]

A search of the American literature covering the period from 1880 to July, 1956, reveals a total of 102 cases reported from the United States, to which can be added the case to be described here. Reports have come from such various parts of the United States as North Carolina,[38] Maryland,[24] Illinois,[45,49] and Pennsylvania.[25] A total of eight cases have been previously reported from the New York area.[10,29,31] Of these, at least three had migrated from the southern states, where most of the cases have been found. The case described in this paper is the first to be reported in the American literature of a Puerto Rican afflicted with ainhum.

The condition is identified with pseudofibrous band formation about the digit, with constriction, rarefaction, and pointing of the distal phalangeal segment on x-ray examination.[44] It eventuates in spontaneous bloodless amputation. A characteristic deep encircling groove or furrow at the level of the digitoplantar fold of the little toe (the most frequent site of involvement) is almost pathognomonic of the disease (Fig. 1). The skin becomes hyperkeratotic, and the walls of the blood vessels may show an endarteritis. There is usually little pain unless secondary infection supervenes.

Ainhum must be differentiated from leprosy, scleroderma, cicatrix formation, and atypical forms of keratoderma.

Davies and Hewer[18] express the belief that epidermophytosis may be of etiologic significance. Among the other theories pro-

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From Department of Surgery and Pathology, New York Medical College-Metropolitan Hospital Medical Center.

Associate Professor of Pathology, Flower and Fifth Avenue Hospitals; Associate Attending Pathologist, Metropolitan Hospital (Dr. Sala). Assistant Professor of Surgery, New York Medical College; Assistant Attending Surgeon, Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Memorial Hospital (Dr. Silverstein).

Figure 1

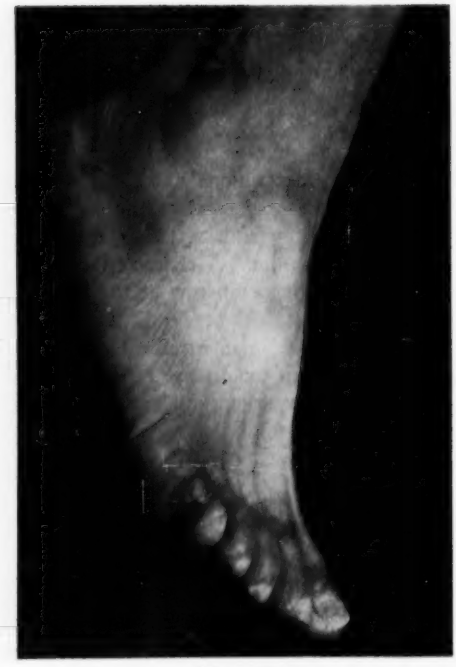


Figure 2

posed are that the disease is a manifestation of leprosy,[56] that the spirochetes of yaws and syphilis are involved,[53] and that the activity of Sarcopsylla penetrans,[52] chronic osteomyelitis,[35] and mechanical causes, such as trauma,[21] may have a part. Endocrine dysfunction has been incriminated.[1] Kean and Tucker, after an exhaustive review,[33] came to the conclusion that . . . "the cause of ainhum is unknown, and its pathogenesis is not clear. . . . the racial factor seems most important." Grschebin[26] believes that "ainhum is not an independent disease with a single, definite cause, but is only a symptom which may arise in many diseases of varied etiology." In general, however, there appears to be a trend toward acceptance of the Matas concept of the disease as a trophoneurosis, eventuating in an annular scleroderma.

Figure 3

The most frequently used treatment, incision of the constricting band, has in general been unsuccessful, and either surgical or spontaneous amputation has occurred.

McKnight treated one case with lumbar sympathectomy.[38] To date, however, no truly efficacious therapy has been described.

Fig. 4.—Epidermophytosis.

Report of Case

A 43-year-old Puerto Rican man was admitted to the Metropolitan Hospital, New York, in no acute distress. The chief complaint was discomfort on walking. The onset of the illness had been gradual and painless and occurred one year prior to admission, in Puerto Rico. The patient denied having ever been out of his country prior to coming to the United States mainland. Inquiries as to possible geneologic factors suggested racial intermarriage of his grandparents, but were not conclusive. No other member of the patient's family or community in Puerto Rico was known to manifest the same or a similar syndrome. The past history was otherwise noninformative.

Figure 5

Physical examination revealed a well-nourished 43-year-old Puerto Rican. The distal extremity of the fifth right toe was enlarged and presented a doughy sensation on palpation. On the flexor surface there was a constriction of the digito-plantar fold, producing the typical deformity of dactylosis spontanea (Figs. 1, 2, and 3). There was no gross evidence of gangrene. The overlying

Figure 6

Fig. 7.—Soft-tissue x-ray.

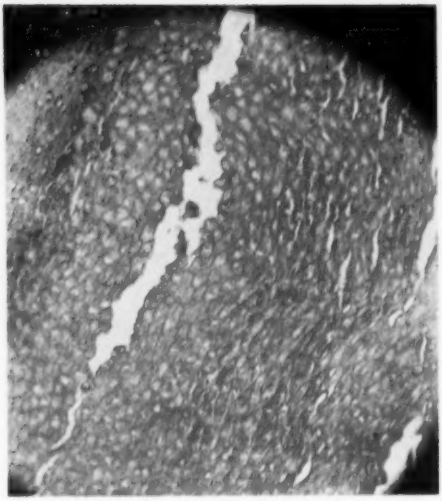


Fig. 8.—Hyperkeratosis of epidermis; reduced to 76% of mag. × 132.

Fig. 9.—Fibrosis and chronic inflammation of dermis; reduced to 76% of mag. × 110.

skin appeared wrinkled (Figs. 1, 2, and 3). Epidermophytosis was present in both feet (Fig. 4). Nontender, hard, movable inguinal nodes were present bilaterally. Examination of the patient did not reveal any other physical abnormalities.

Thermocouple readings, oscillometry, nasal smears for Mycobacterium leprae, urinalysis, and serology and other blood studies were all within the normal range. X-ray examination (Figs. 5, 6, and 7) revealed pointing in the midthird of the proximal phalanx of the right fifth toe, with constriction of the soft tissues at this point.

Because of the complaint of difficulty in walking, the digit was amputated.

Histopathologic examination of the specimen revealed fibrosis of the dermis and deeper tissues, with marked atrophy of the bone between the indentations of the skin. The epidermis was markedly hyperkeratotic, with a normal-appearing basal layer. The corium at the site of constriction was practically bereft of papillae. At the margin of the ring there was dense infiltration of the corium with round cells. Away from the site of constriction the papillae were elongated and narrow.

Fig. 10.—Fibrosis and chronic inflammation of dermis; reduced to 76% of mag. × 132.

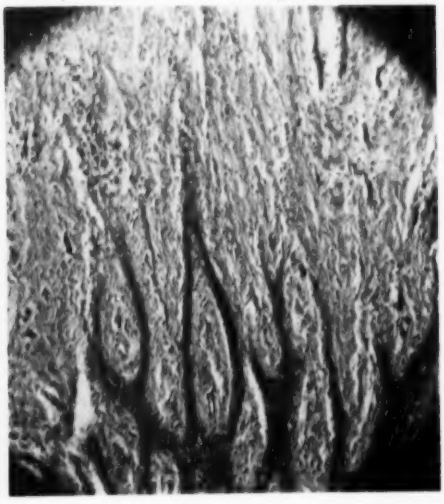
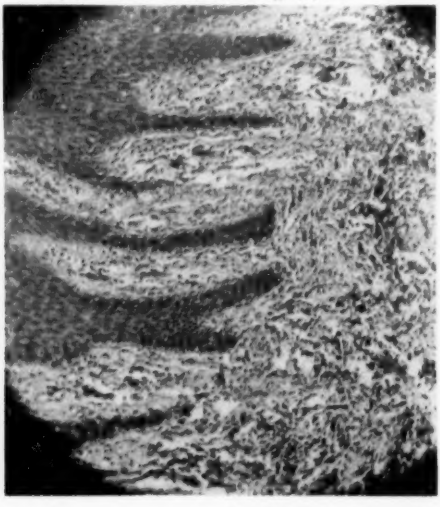


Fig. 11.—Fibrosis and chronic inflammation of dermis; reduced to 76% of mag. × 132.



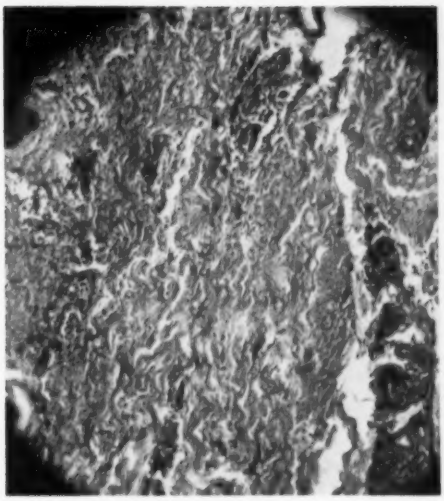


Fig. 12.—Fibrosis of corium; reduced to 76% of mag. × 132.

Fig. 13.—Simple bone atrophy; reduced to 76% of mag. × 132.

The vessels and nerves were found to be normally present.

The salient histologic features were hyperkeratosis of the epidermis (Fig. 8), fibrosis and chronic inflammation of the dermis (Figs. 9, 10, and 11), fibrosis of the corium (Fig. 12), and simple bone atrophy (Fig. 13).

Summary

A case of ainhum in a 43-year-old Puerto Rican man is presented, together with photographs, x-rays, and photomicrographic sections.

New York Medical College, Flower and Fifth Avenue Hospitals (Dr. Silverstein).

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Fate of Experimental Arterial Implants into the Right Ventricle

DAVID C. SABISTON Jr., M.D., and JEAN P. FAUTEUX, M.D., Baltimore

Numerous investigators have conducted a variety of studies directed toward revascularization of the heart. Of the procedures attempted, most fall into one or more of the following groups: (1) the introduction of an irritant in the pericardium; (2) the grafting of other organs or tissues to the surface of the heart; (3) the anastomosis of a systemic artery to the coronary sinus, and (4) the implantation of a systemic artery into the left ventricular myocardium. The last mentioned of these procedures was introduced by Vineberg and associates, and they have reported encouraging results both in the experimental animal and in man.[7,8] Their experimental findings have been confirmed by some,[2] whereas others have obtained different results.[3,5,6,8] In all of the work yet reported on arterial implants into the myocardium the implants have been placed into the left ventricle. In this communication the studies concern similar arterial implants into long tunnels in the right ventricle.

Methods

Twelve adult mongrel dogs were used. After premedication with morphine and atropine, anesthesia was induced with ether, and an endotracheal tube was inserted. Positive-pressure anesthesia was maintained by the use of a mechanical respirator. An incision was made in the left side of the neck, and the common carotid artery was freed from the vagus nerve. The internal and external carotid vessels were exposed, ligated, and divided. The chest was entered through the left fourth intercostal space, and the mediastinal portion of the carotid artery was mobilized and the entire vessel was delivered into the chest. An arterial clamp was placed on the proximal portion of the carotid artery, and several perforations were made in the wall. The ligatures on the branches were removed and the ends left open. The pericardium was opened and a suture placed at the apex of the heart. The heart was supported posteriorly with the finger, and with traction on the apical suture a small incision was made at the apex. An Adson clamp was inserted through the opening and advanced upward through the midthickness of the anterior wall of the right ventricle, emerging at the base of the pulmonary artery. The tip of the carotid was then grasped in the clamp and drawn into the ventricular tunnel and sutured at the apex (Fig. 1). The occluding clamp was then removed and the vessel allowed to pulsate. The right coronary artery was then dissected at its origin and doubly ligated and divided.

At the time the animal was killed, several procedures were performed in an effort to evaluate the state of the implanted artery and the establishment of possible vascular communications with the normal coronary arterial system. The details of these procedures have been discussed in another communication[6] and will not be repeated here. For determination of the volume of blood flow through the implant the vessel was exposed through the left chest, employing the same anesthetic technique as that during the original procedure. Mean arterial pressure was recorded with a Statham gauge connected to a Sanborn Poly-Viso recorder. The carotid artery was cannulated at its entry into the myocardium and perfused from a constant-pressure system with saline or heparinized blood (Fig. 2). The patency and vascular communications of the implant were demonstrated by the injection of a solution of sodium iodide, and a roentgenogram of the speci-

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From the Department of Surgery, The Johns Hopkins University School of Medicine and Hospital.

Assistant Professor of Surgery, Department of Surgery, The Johns Hopkins University School of Medicine and Hospital; Investigator, Howard Hughes Medical Institute (Dr. Sabiston). Present address (Dr. Fauteux): Hotel Dieu, Montreal, Canada.

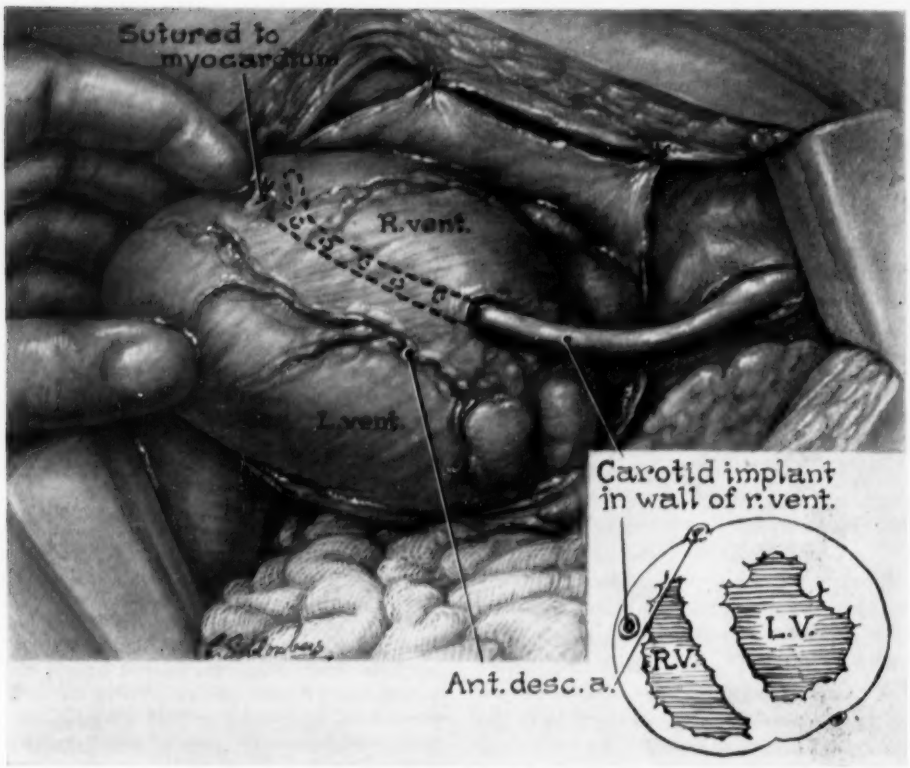


Fig. 1.—Illustration of method employed in implanting carotid artery into the right ventricle.

men was taken. The heart was fixed in formalin, and blocks were taken of the implant at entry into the myocardium, in the midmyocardium, and at the apex. Tissue sections were stained with hematoxylin and eosin, the Verhoeff-Van Gieson elastic tissue stain, and ferric ferrocyanide (Gomori).

Results

Of the 12 animals, 9 survived the operative procedure and were observed over a period of 39 to 86 days (average 65 days). Three died during the procedure of ventricular fibrillation following ligation of the right coronary artery. In six of the nine chronic survivors the carotid implants were grossly patent at the time the animals were killed. In the remaining dogs the implant was thrombosed. In five of the specimens in which the implants were grossly patent a solution of sodium iodide was injected into the carotid, and communications were demonstrated with the normal coronary arterial system (Fig. 3). In two of these the right ventricular cavity filled immediately, indicating direct communication with the graft.

The volume of flow through the patent arterial implant was determined in six animals by perfusion of the graft at a constant pressure with saline or blood. At a mean pressure of 100 mm. Hg the flow in the respective animals was found to be 1.6, 2, and 3.2 cc/min. In the other three the flows were 17.6, 32, and 52.4 cc/min. However, in the latter animals direct communication of the implant with the right ventricular cavity was demonstrated and was undoubtedly responsible for the high volume of flow.

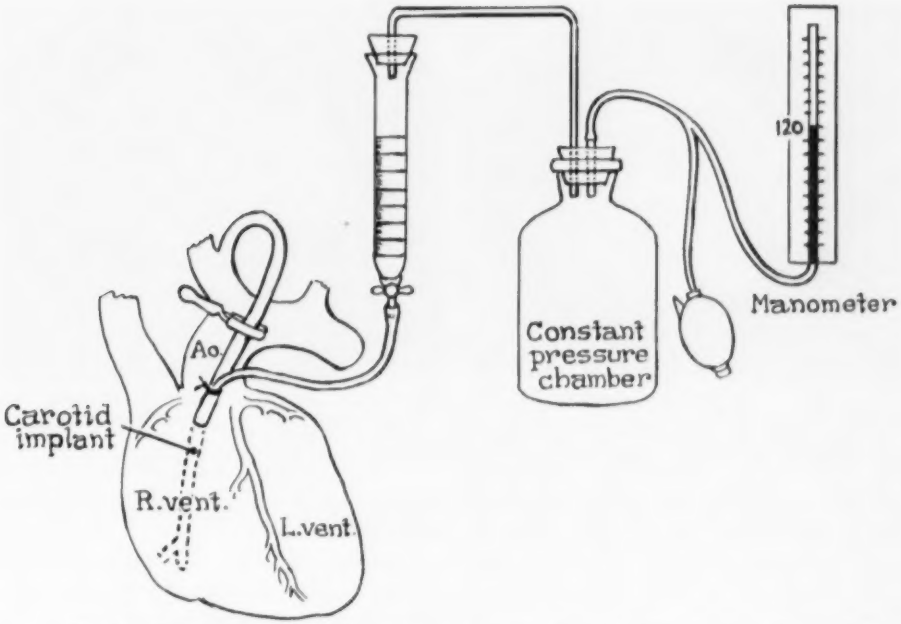
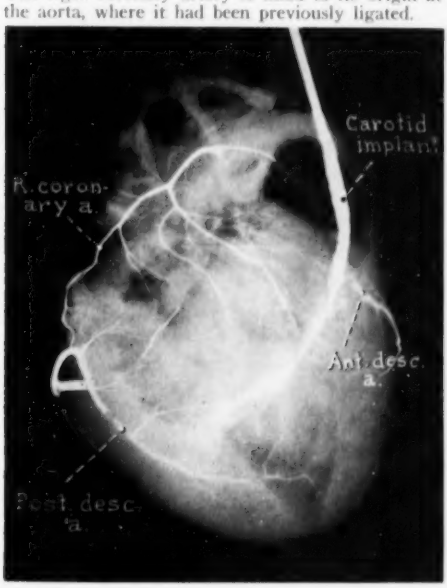


Fig. 2.—Diagrammatic illustration of technique employed for determination of volume of flow through the carotid implant.

Fig. 3.—Roentgenogram of heart with carotid artery embedded in the right ventricle. The implant has been injected with a solution of sodium iodide and the anterior descending and posterior descending coronary arteries are well visualized. The right coronary artery is filled to its origin at the aorta, where it had been previously ligated.



At the time of killing healed infarcts were present in the right ventricle of six of the nine animals that were chronic survivors. Histologic sections of the implanted vessel showed a relatively normal arterial wall, slight intimal thickening, or thrombosis (Fig. 4).

Comment

The implantation of a systemic artery into the myocardium was first reported by Vineberg in 1946.[7] Since that time several groups of investigators have studied this type of preparation, and their results have been both confirmatory and conflicting.[2,3,5,6,8] In his studies, Vineberg placed the internal mammary artery into a short tunnel in the left ventricle. In recent work in our laboratory we have employed a vessel of large diameter (carotid) and have implanted it into a tunnel the entire length of the left ventricle. The results of these experiments demonstrated that under these circumstances the implants remained patent in a high per-

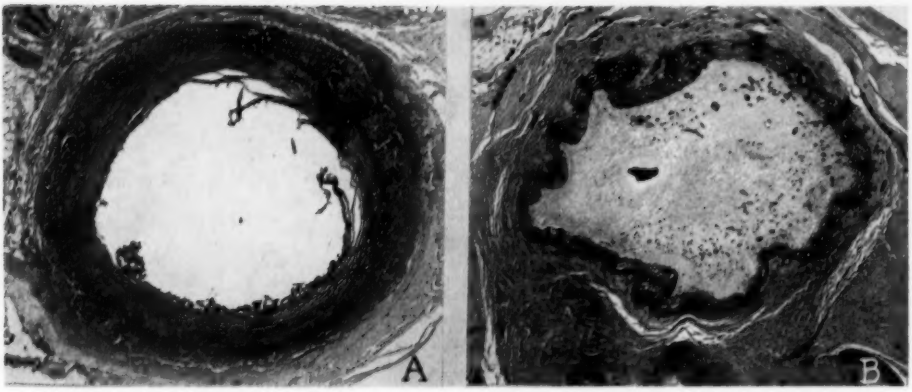


Fig. 4.—*A*, photomicrograph of carotid implant into the ventricle, showing patent lumen at 39 days. Verhoeff-Van Gieson stain; × 20. *B*, photomicrograph of carotid implant into right ventricle with thrombosis and microscopic recanalization demonstrated by injection of India ink at 81 days. Verhoeff-Van Gieson stain; reduced to 78% of mag. × 25.

centage of animals and offered protection against subsequent deliberate myocardial injury.[5] Despite these facts, measured blood flow through the implant to the heart was usually small.

The studies on arterial implants into the myocardium reported in the literature thus far have concerned implants into the left ventricular myocardium. Since the pressure within the right ventricle is considerably less than that in the left ventricle, it is possible that this factor could influence the fate of an arterial implant. As an extension of previous work, the present experiments involve the use of a large vessel (carotid) implanted into long tunnel into the right ventricle. The results showed that 60% of the arterial implants remained grossly patent. This figure may be compared with the results obtained in our previous study, in which it was shown that similar implants into the left ventricle remained patent in 92% of the animals.[6]

In the present experiments the coronary perfusion studies and arteriograms indicated that definite arterial communications developed, but the volume of blood flow through them was small. Histologic study of some of the implanted vessels showed definite thickening of the arterial wall, thought to be due to organization of thrombus material on the vessel wall. These findings are similar to those in the study of implants into the left ventricle.[6]

The explanation for the continued patency of the majority of arterial implants within the ventricular myocardium cannot be stated with certainty. However, in previous work we have shown that similar implants into organs such as the sternocleidomastoid muscle, spleen, and liver result in an early thrombosis of the vessel.[6] These findings at least suggest that the rhythmical contraction of the ventricle is responsible for the persistent patency of implants into the heart. Further, the force of contraction is considerably greater in the left ventricle than in the right ventricle and may explain that somewhat higher incidence of patent implants in the former.

Summary

In an experimental study the carotid artery was embedded into a long tunnel into the right ventricle. This vessel continued to be patent in approximately two-thirds of the animals and became thrombosed in the remainder. Vascular communications could be demonstrated between the patent implant and the coronary arterial system, although the volume of flow through the implant as determined by direct perfusion was small. As compared with a previous

study, the incidence of patency of arterial implants into the right ventricle is less than similar implants into the left ventricle. This is probably due to the difference in intramyocardial pressure of the two ventricles.

The Johns Hopkins Hospital (5).

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Scientific Exhibits

Esophageal Reconstruction by Esophagojejunostomy and Esophagocologastrostomy

Procedures with Special Reference to Lye Strictures

LEWIS H. BOSHER Jr., M.D.
ALFRED M. DECKER Jr., M.D.
and
JAQUELIN M. HARRISON, M.D.
Richmond, Va.

The problem of reconstitution of alimentary tract continuity within the thorax remains dynamic. Procedures in common usage pose the problems of peptic regurgitation, multiplicity and complexity of operations, nutritional defects, and recurrent stricture formation.

As many of these difficulties appear to have been overcome by the use of esophagojejunostomy and esophagocologastrostomy via an anterior mediastinal tunnel, an experience with these operations is thought worthy of presentation.

This exhibit demonstrates in some detail the operative techniques and their application to selected benign and malignant esophageal lesions.

From the Medical College of Virginia, Hospital Division.

Shown as a scientific exhibit at the 48th Annual Meeting of the Southern Medical Association, St. Louis, Nov. 8-11, 1954.

O. O. Age 18 months. Lye burn June 28, 1953. Gastrostomy July, 1953. Esophagocologastrostomy completed October, 1953, in two stages.

Fig. 1.—Esophageal obstruction 16 days after burn, later developing into complete stricture.

Fig. 2.—Ten weeks after completion of reconstruction.

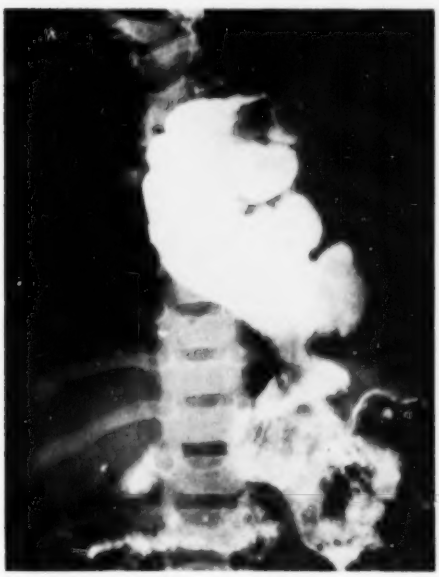


Fig. 3.—Effective peristalic wave carrying barium rapidly to stomach.

Fig. 4.—Low position of esophagogastrostomy on anterior stomach wall.

Fig. 5.—Postmortem examination showing position of anterior mediastinal colon tube.

R. R. Age 53 years. Carcinoma of the esophagus, middle third. Palliative reconstructive procedure attempted. Death on second postoperative day, of adrenal insufficiency (?).

Fig. 6.—Left colic artery passing behind stomach.

Fig. 7.—Unexpected pathology seen in gangrene of mucosa of distal colon (colocolostomy).

Fig. 8.—Lye stricture in midthird of thoracic esophagus two months after burn.

B. J. Age 2 years. Lye burn September, 1953. Gastrostomy October, 1953. Esophagocologastrostomy in one stage, May, 1954.

Fig. 9.—Three weeks after one-stage reconstruction.

Fig. 10.—Isoperistalic tube utilizing peristaltic propulsion.

H. P. Age 16 years. Lye burn December, 1949, followed by stricture and tracheoesophageal fistulas. Pharyngojejunostomy completed October, 1951, after multiple stages.

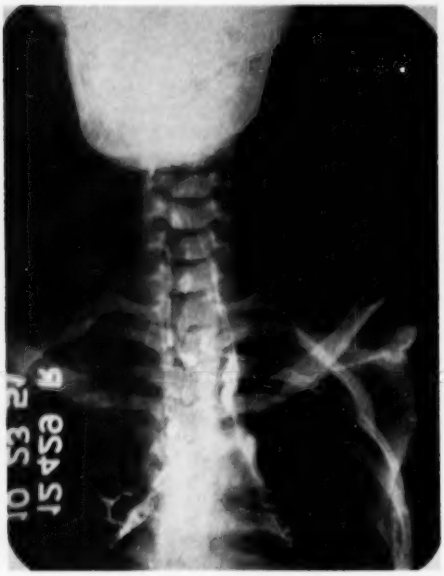


Fig. 11.—Very high stricture associated with tracheoesophageal fistulas, resulting from mediastinitis.

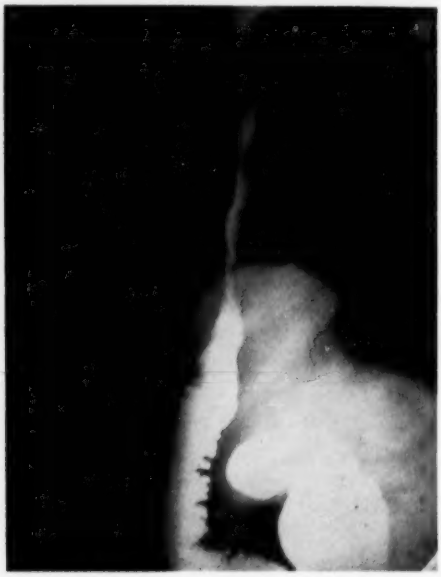


Fig. 12.—Failure of initial jejunal tube, with sloughing of upper 6 in., August, 1950.

Fig. 13.—Three months following remobilization of jejunum and pharyngojejunostomy.

Fig. 14.—Twenty months after reconstruction. Note loss of haustral markings in upper tube.

W. R. Age 11 years. Lye burn and complete stricture at age of 15 months (1952). Gastrostomy (1942). Jejunal tube implanted in superior mediastinum February, 1953, with cervical esophagojejunostomy 15 days later.

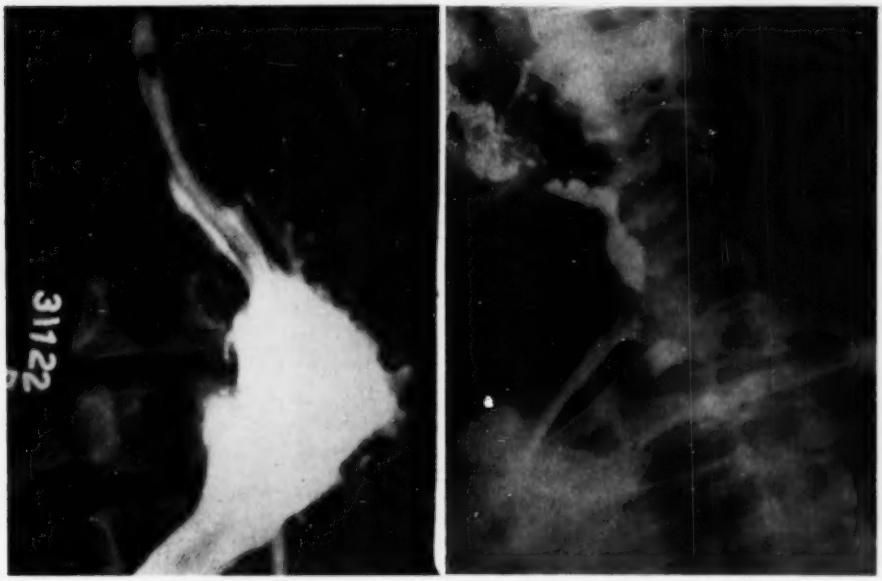


Fig. 15A and Fig. 15B.—Filling with iodized oil (Lipiodol) from above and below shows limits of complete stricture.

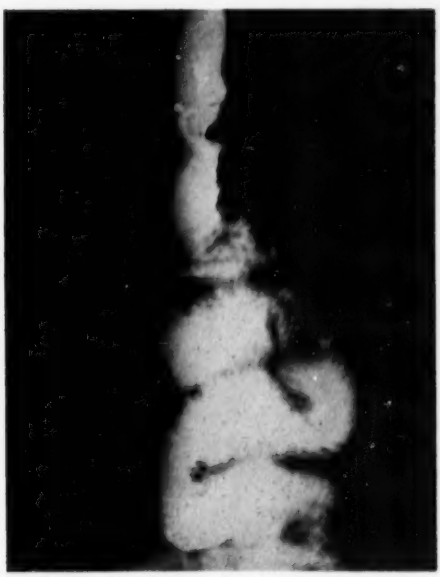


Fig. 16.—One year after completion of two-stage reconstruction.

Fig. 17.—Loss of haustral markings in upper tube.

F. J. Age 19 years. Lye burn August, 1951, followed by stricture. Cervical esophagojejunostomy completed September, 1953, after multiple stages.

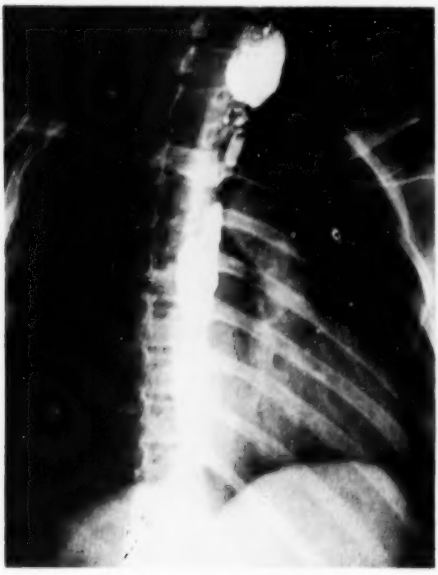


Fig. 18.—High stricture one year after burn.

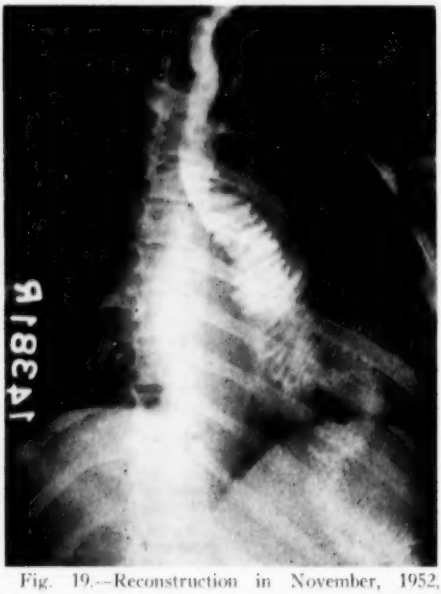


Fig. 19.—Reconstruction in November, 1952, showing some residual stricture due to incomplete removal initially.

J. C. Age 52 years. Carcinoma of the esophagus, middle third. One-stage cervical esophagojejunostomy, followed by fistula formation and rapid healing. Esophagectomy performed as secondary procedure.

Fig. 20.—Nearly complete obstruction due to malignancy.

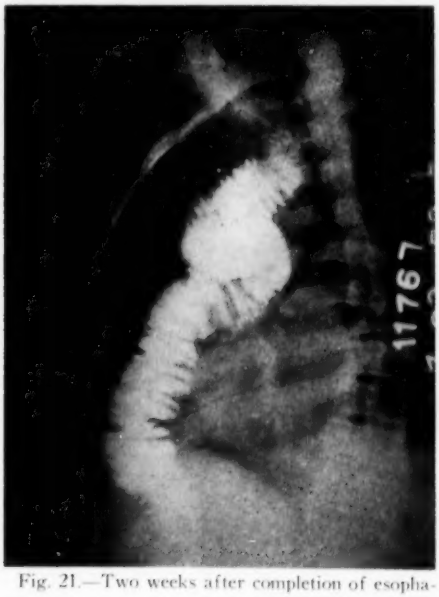
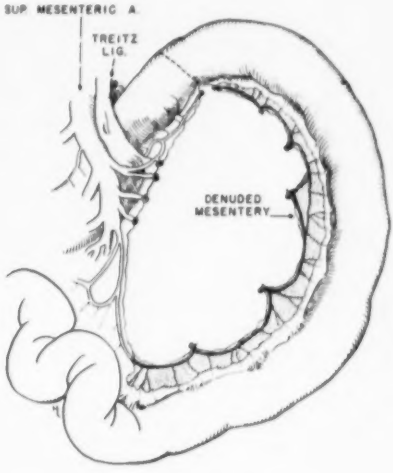
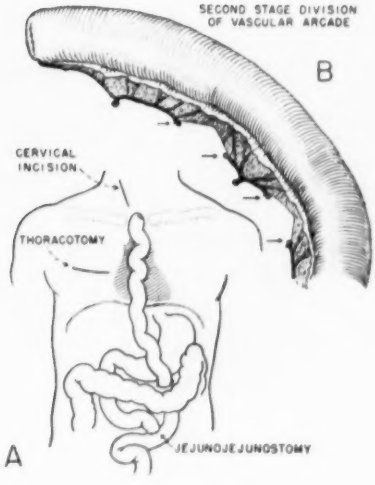


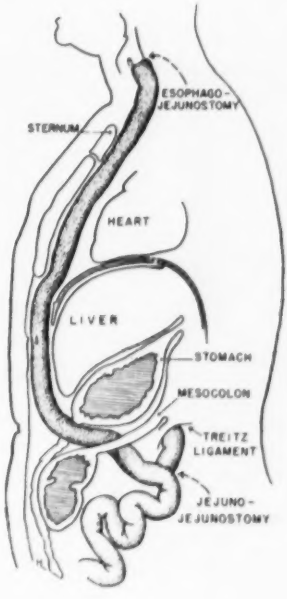
Fig. 21.—Two weeks after completion of esophagectomy.

Esophagojejunostomy

An isoperistaltic jejunal tube, prepared by division of the first three mesenteric vessels, is drawn through an anterior mediastinal tunnel. The cervical esophagojejunostomy is customarily performed at a second stage, at which time additional length may be gained by division of the vascular arcade of the implanted jejunum. For benign lesions the distal divided cervical esophagus is closed and left in situ. Jejunogastrostomy in addition may be desirable.

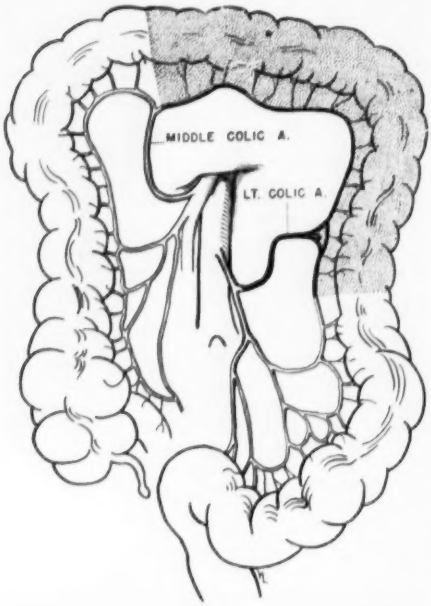


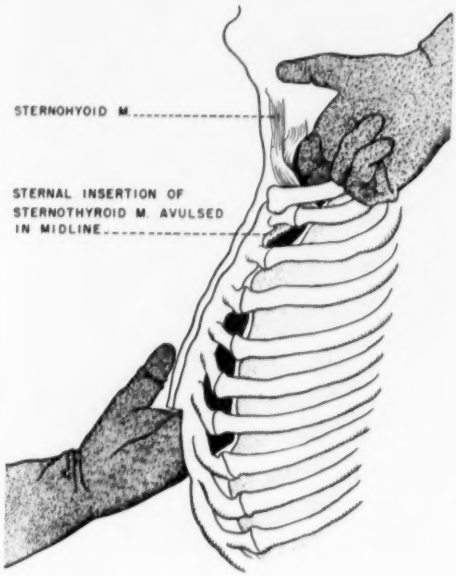


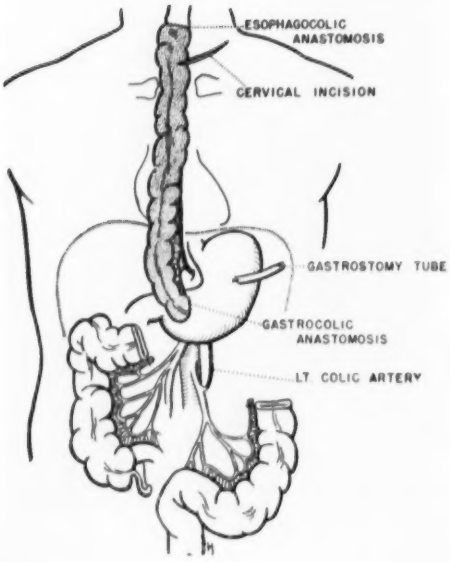


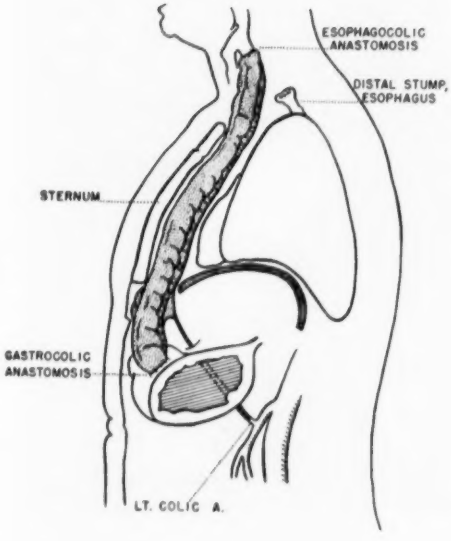
Esophagocologastrostomy

An isoperistaltic tube supported by the left colic artery is formed from transverse and descending colon and drawn up the anterior mediastinum. Intestinal continuity is completed without staging by cervical esophagocolostomy, distal cologastrostomy, and colocolostomy. Adequate length and blood supply have thus far not presented a problem.









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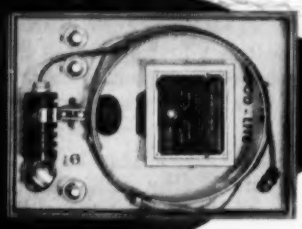

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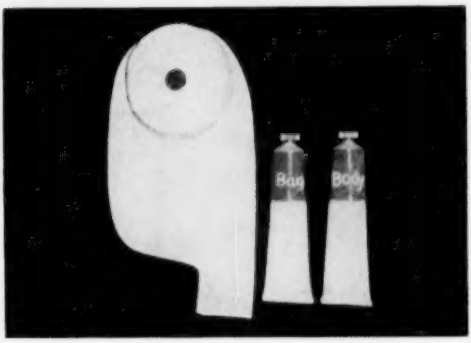

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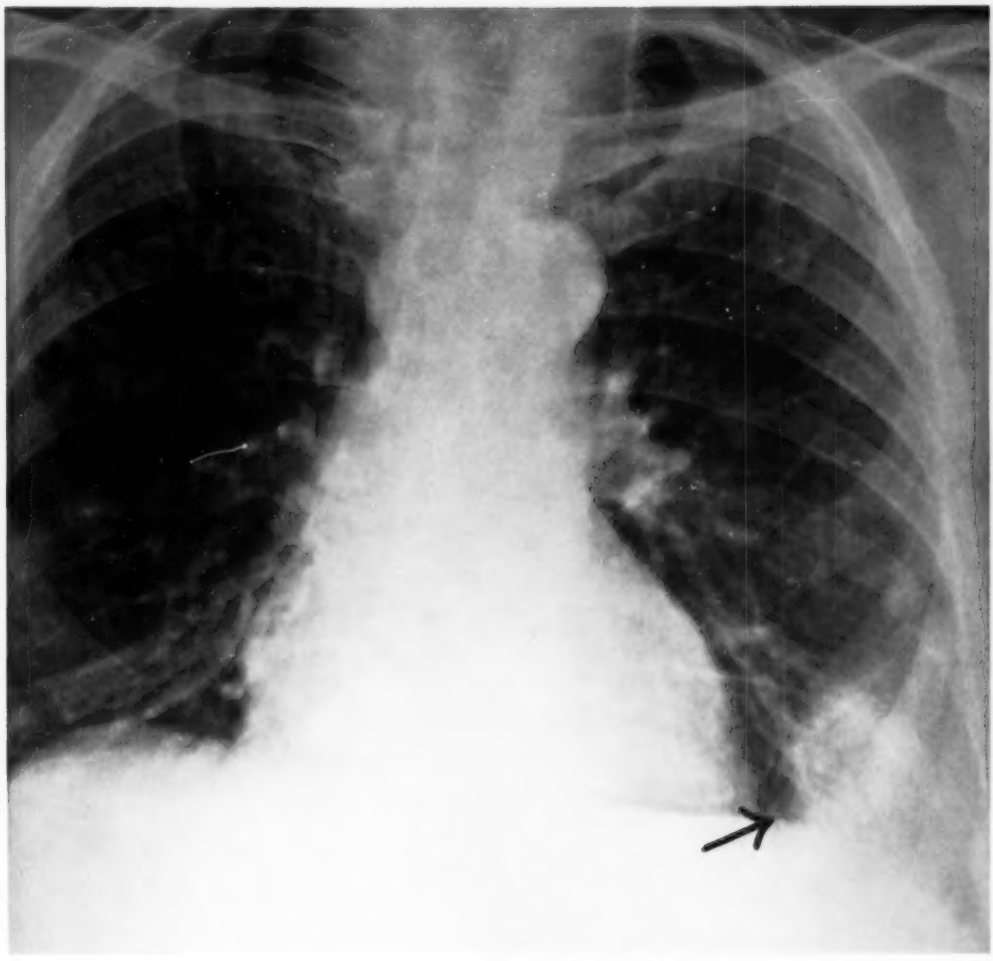

EXCISION OF LIPOMA OF PARIETAL PLEURA. 1. Preoperative radiograph, A-P view, indicates presence of mass within pleural cavity.

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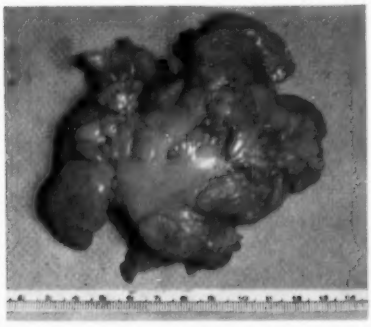

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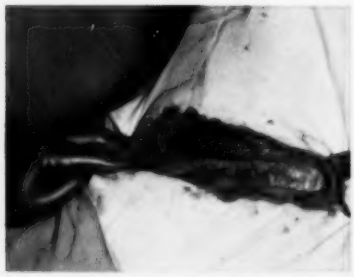
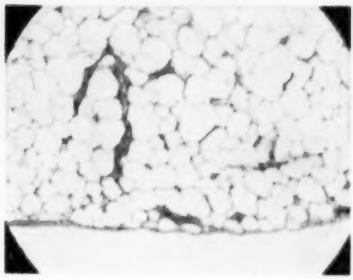
3. Laminagraph establishes position of mass in chest. It also suggests its physical characteristics.



4. Left thoracotomy. Eighth rib is exposed.

5. Mass attached to left parietal pleura is exposed.



6. Photomicrograph of mass—a lipoma or fatty, benign neoplasm. (Magnification, X40.)

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1. Spencer, H.; Berger, E.; Charles, M.; Gottesman, E. D., and Laszlo, D.: Effects of 17-alpha-Ethyl-17-Hydroxy-Norandrostenone, Proc. Am. A. for Cancer Res. 2:149 (April) 1956.

2. Proceedings of a Conference on the Clinical Use of Anabolic Agents, Chicago, Illinois, Searle Research Laboratories, April 9, 1956.

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